

ATTENUATION CORRECTION METHODS FOR
POSITRON EMISSION TOMOGRAPHY

By
CHEN-HSIEN WU

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Dedicate to my parents,
Mr. Min-Ming Wu and Ms. Jau-Jr Wu,
and my sister,
Hwa-Yu.

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By

Chen-Hsien Wu

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Positron emission tomography (PET) is an imaging modality that provides biochemical information about the human body. Among the sources of error in PET, attenuation is the one that impacts image quality the most. The standard method for correcting attenuation consists of the following two step procedure. First, a blank scan and transmission scan are used to estimate the survival probabilities. Then, the data for each pair of detectors is divided by the corresponding survival probability estimate. This corrected data and a reconstruction algorithm, such as

the filtered back-projection algorithm, are then used to generate an estimate of the emission intensity, which is displayed as an image.

In this dissertation, two iterative methods are proposed for correcting attenuation errors in PET. The first method is a maximum likelihood (ML) method that simultaneously estimates the emission intensity and attenuation density. The second one is a least squares (LS) reprojection method, where the survival probabilities are estimated by reprojecting a LS estimate of the attenuation density. The emission intensity is estimated using the expectation maximization maximum likelihood (EMML) algorithm with a probability matrix that has been modified by the survival probability estimates. Both methods are guaranteed to produce non-negative estimates of the emission intensity and the attenuation density, provided that the initial estimates are nonnegative.

From simulation studies, it appears that the major advantage of the proposed methods over the standard method with the filtered back-projection algorithm is that they (1) have less noise, (2) do not have artifacts outside the region of interest, and (3) they provide high quality images even for short transmission scans (less than 10 minutes).

CHAPTER 1

INTRODUCTION

For both clinical and research applications, medical imaging modalities are used to obtain important information on the functionality and anatomy of the human body. Imaging modalities such as X-ray computed tomography and magnetic resonance imaging provide detailed images of the anatomical structure of the body. However, in many applications, it is more beneficial to have a modality that determines *functional information* such as blood flow rates, oxygen utilization rates, and glucose utilization rates within the region-of-interest (ROI) (e.g., brain, heart) [28]. For example, glucose utilization rates are used in oncology to diagnose tumors and to determine the efficacy of a treatment.

Functional information on the human body can be obtained using (1) positron emission tomography (PET), (2) single-photon emission computed tomography (SPECT) [16], and (3) functional magnetic resonance imaging [51]. Among them, PET is probably the most flexible imaging modality. For example, PET can image which parts of the brain are functioning while a subject is performing a speaking tasking. This is not possible in functional magnetic resonance imaging because the scanners are too loud [55]. An advantage of PET over SPECT is that the radionuclides in PET can be incorporated into molecules (or analogs) of biological interest [56].

In this dissertation, we propose two methods for correcting a certain error in PET called *attenuation*. The outline of the dissertation is as follows. An overview of PET is provided in the remainder of Chapter 1. In Chapter 2, we discuss the physics behind PET, introduce a mathematical model for the data, and review existing attenuation correction methods. We introduce the proposed maximum likelihood and least-squares reprojection methods in Chapter 3 and Chapter 4, respectively. In Chapter 5, we investigate the performance of these methods using synthetic and real data. Finally, we discuss our conclusions and future research direction in Chapter 6.

1.1 Overview: Positron Emission Tomography

PET is exceptional in its capability to quantitatively determine functional information within a ROI. Since George Hevesy won a Nobel Prize for his pioneering research on radionuclides in 1943, numerous researchers have investigated methods to obtain functional information on the human body. However, the first PET machine was not built until 1975 by Michael Phelps, Edward Hoffman, and their colleagues [42]. Since then, scientists and engineers have made significant advances in the hardware, radionuclides, and reconstruction algorithms used for PET. In Fig. 1.1 is a PET scanner of the Quest series from the GE Medical Systems.

We first introduce the major components of a PET scan, which are as follows:

1. A compound is labeled with a radionuclide.



Figure 1.1. Quest 250 from GE Medical Systems (courtesy of GE Medical Systems)

2. The labeled compound or *radiopharmaceutical* is introduced into the subject's body.
3. The data are collected.
4. An image is produced that represents the concentration of the radiopharmaceutical within the ROI.

Radionuclides in PET are (1) incorporated into compounds that are naturally used by the body, (2) emit positrons, and (3) have short half-lives. A radionuclide's half-life must be sufficiently long so that there is enough data to get quality images [38]. The most common radionuclides in PET include ^{11}C , ^{15}O , and ^{13}N , which are used to label glucose, water and amino acid, respectively. The most widely used radiopharmaceutical is ^{18}F -labeled deoxyglucose (FDG), which is used to study glucose metabolism. Because of the short half-lives of positron-emitting radionuclides (2 minutes, 10 minutes, 20 minutes, and 110 minutes for ^{11}C , ^{15}O , ^{13}N , and ^{18}F , respectively), they need to be produced on-site using a cyclotron. The cyclotron creates radionuclides by smashing the atomic shell of certain molecules with protons. Cyclotrons are expensive and costly to maintain because they require at least two operators.

SPECT uses radionuclides, such as ^{99m}Tc , ^{201}Tl , and ^{123}I , which have half-lives that range from 10 hours to several days. Because of their long half-lives, radionuclides in SPECT can be made in advance and shipped to hospitals so an on-site cyclotron is unnecessary. However, long half-lives mean that patients are exposed to radioactivity for long periods.

After being administered to a subject, the labeled compound will localize in the ROI. For example, FDG is absorbed preferentially by the brain because glucose is a source of energy [11]. Another example is the use of ^{15}O based radiopharmaceuticals to index injured tissues by monitoring the oxygen metabolism of tissues [52].

1.2 Emission Data

As mentioned previously, the radiopharmaceutical localizes in the ROI. When the radionuclide decays, it emits positrons which travel a short distance (3-4 mm) before annihilating with nearby electrons. The areas with a high concentration of the radiopharmaceutical emit more photons than the areas of low concentration. When a positron annihilates with an electron, two high-energy (511 keV) photons are produced that fly off at an almost 180-degree angle from each other. This annihilation process is shown in Fig. 1.2. The photons go through the subject and are registered by rings of detectors surrounding the subject. When two detectors detect a pair of photons within a short period of time, these photons are said to be in *coincidence* (see Fig. 1.2). For each pair of detectors, there is a count that corresponds to the number of observed coincidences. The *emission data* is the collection of these counts.

From the emission data, we can estimate the concentration of the radiopharmaceutical using a reconstruction algorithm. A computer is then used to display images where the intensity is proportional to the estimated concentration of the radiopharmaceutical. In the next section, some clinical and research applications of PET will be presented.

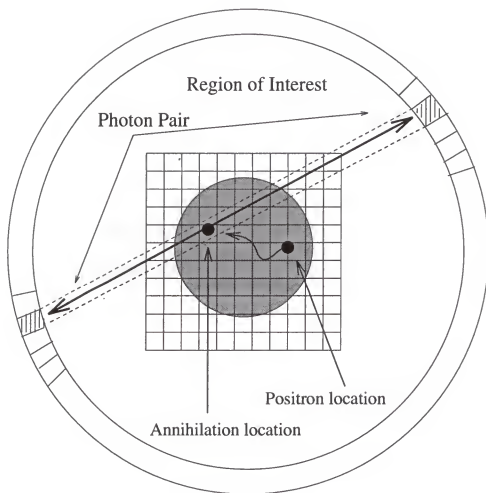


Figure 1.2. A positron travels a short distance and annihilates with a nearby electron to produce a pair of photons that fly off at 180-degree angle. These photons are detected by a ring of detectors

1.3 Clinical and Research Applications

PET is widely used in pathology and oncology because it can quantitatively measure blood flow, and utilization rates of glucose, CO_2 , and fatty acid ammonia. PET provides functional information about tissues or organs, which cannot be obtained by modalities such as magnetic resonance imaging and computed tomography [52]. It is also a powerful tool for investigating brain functions such as emotion, thinking, vision, and speech [5, 30]. Since the major energy source of the brain is glucose, FDG is used to map the brain's energy consumption. In other words, if a specific region of the brain has increased functionality, then the regional blood flow increases to provide the necessary energy. As a result, the concentration of the radionuclide used in FDG increases in that region. Using PET to map the concentration of the radionuclide, we can observe the higher functionality in that region of the brain. Based on the concepts discussed above, scientists have used PET images to assess the brains of normal children and children under abuse. They found that the children who were abused had slower developments in brain functions such as speech and vision as compared to normal children [7].

PET has clinical applications as well. For example, PET has the ability to measure the size of infarcts in the heart after a coronary attack, to diagnose diseases such as Alzheimer's [45] and epileptic seizures [36], and to survey the effects of treatments such as radiation therapy, chemotherapy, and hormone therapy. In addition, whole-body PET is used to spot metastases, which is very difficult for other modalities because of the small sizes and the random occurrences of metastases inside cancer patients' bodies. The effect of the chemotherapy on cancer

patients can be evaluated by visualizing the sizes and locations of metastases on PET images [1].

PET is also used in psychological studies. For instance, it was used in the early 1990s several times by courts in California to determine whether neural malfunctions in the brain caused a suspect's violent behavior. Another interesting experiment was the monitoring of six bank officials' brain functions when they were exposed to a video of an armed bank robbery. This was done to find out the connection between stress and visual re-experience [22].

1.4 Advantages and Disadvantages

PET is a better imaging modality than SPECT in the sense of offering better efficiency, sensitivity, and accuracy as compared to SPECT [11]. Also, unlike SPECT, the radionuclides used in PET are easily incorporated into compounds, such as glucose, that are naturally used by the body. Using different radionuclides, PET is able to image different biochemical activities while functional magnetic resonance imaging only can image hydrogen activity. Additionally, PET can track chemical changes that do not affect blood flow enough for functional magnetic resonance imaging to measure.

Unfortunately, PET has some major disadvantages such as its high cost, high complexity, and the requirement of highly skilled personnel. The cost of a PET scanner is similar to a magnetic resonance imaging scanner. However, the cyclotron used to generate the radionuclides is also very expensive. Additionally, at least three skilled professionals – one to maintain the scanner, one to run the

cyclotron and another one to produce radionuclides – are needed to operate a PET laboratory. For SPECT, it is not necessary to create the radionuclides on site because the radionuclides used in SPECT can be stored. Even though its image quality is not as good as that of PET, SPECT is more widely available in practice because it is significantly cheaper.

CHAPTER 2 BACKGROUND

In this chapter, we review the basic physics of PET, introduce the Poisson model, and discuss sources of errors in the data. Since the focus of this dissertation is attenuation correction, we also review existing attenuation correction methods.

2.1 Basic Physics of PET

As discussed in Chapter 1, the subject is given a radiopharmaceutical that emits positrons. When a positron annihilates with a nearby electron, two photons are produced that depart at an angle near 180 degrees. The region of interest (ROI) is surrounded by rings of detectors that detect the photons. We will use the term *tube* to refer to a pair of detectors. When a pair of photons is incident on a tube within a small time interval, a counter is increased (see Fig. 2.1). The emission data are the counts associated with the various tubes.

The detectors are shielded from radiation coming from outside the region of interest by heavy lead rings at the front and back of the gantry. In order to switch between the slice-collimated mode and the three-dimensional mode, most commercial PET scanners contain spherical thin interplane rings called *septa*. When the scanner is in slice-collimated mode, the septa only allows in-plane tubes to detect photons. When a scanner operates in full three-dimensional mode, the

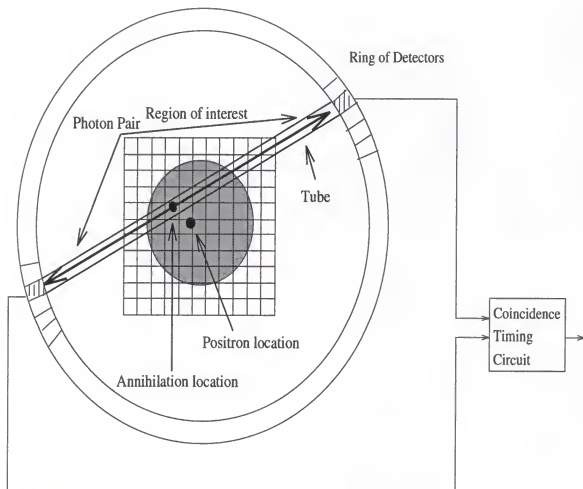


Figure 2.1. Annihilation Process

septa are withdrawn to permit photons to be registered by in-plane tubes and cross-plane tubes [37].

A detector module consists of an array of crystals coupled to several photomultiplier tubes. In Fig. 2.2, a detector module of the Scanditronix PC4096-15WB whole-body PET scanner is shown. A detector ring contains several hundred detector modules (e.g., 384 for the Siemens-CTIECAT EXACT 921 scanner). When a crystal is hit by a 511 keV photon, it interacts with the photon and generates numerous light photons. Then, the light guide connected to the crystal transfers the light photons to the nearest photomultiplier tube (PMT). The PMTs collect light photons and convert them into electrical signals that are stored in a computer. The outputs of the PMTs are decoded to determine which detector module was hit by a photon. The most widely used crystal material is Bismuth-Germanate because it has good properties when it interacts with 511 keV photons such as a high light photon producing rate, short decay time, and a fast energy rise time [26].

Once the data is collected, algorithms are used to reconstruct the PET images. The most popular method is the filtered back-projection algorithm [45]. It is extremely fast and easy to implement, but the images are noisy, have negative values, and contain artifacts outside the ROI. Alternative approaches include statistically based methods such as maximum likelihood [28, 46], maximum a posterior [20, 21, 30, 31], least squares [15, 40, 24, 46, 49, 50], and weighted least-squares [3, 12, 17] methods. An advantage of statistically based methods is that they account for the errors in the data and do not have artifacts outside the ROI. A disadvantage of them is that they are computationally demanding.

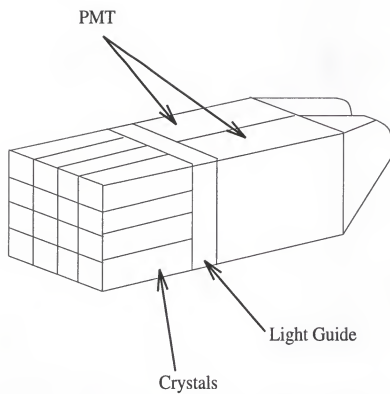


Figure 2.2. Scanditronix PC4096-15WB detector module: 16 crystals, 1 light guide, and 2 dual cathode PMTs

2.2 Poisson Model

Since the data collection in PET is actually a photon counting process, it is reasonable to assume that the emission process is a Poisson process with unknown mean [38]. Based on this assumption, Shepp and Vardi proposed a model called the *Poisson model* [46] in 1982. Their model assumes that the data is error free and obeys a Poisson process.

In the Poisson model, the ROI is discretized into a grid of J voxels. Let N_j denote the number of emissions in voxel j , where N_j is assumed to be Poisson with unknown mean $x_j \triangleq E[N_j]$. Let Y_i denote the number of coincidences detected in the i^{th} tube, where Y_i is assumed to be Poisson with mean $d_i \triangleq E[Y_i]$ and I is the number of tubes. It is also assumed that (1) $\{N_j\}_1^J$ are independent, (2) $\{Y_i\}_1^J$ are independent, and (3) the probability that an emission in voxel j is detected in the i^{th} tube, P_{ij} , is known for all i, j . Under these assumptions, it can be shown that the mean of the i^{th} tube is given by

$$d_i = \sum_{j=1}^J x_j P_{ij} \quad (2.1)$$

$$= (\mathbf{P}\mathbf{x})_i, \quad i = 1, 2, \dots, I, \quad (2.2)$$

where the $(i, j)^{\text{th}}$ element of $\mathbf{P}$ is P_{ij} and $(\mathbf{P}\mathbf{x})_i$ denotes the i^{th} element of the vector $\mathbf{P}\mathbf{x}$.

Given the data, $y_1, y_2, \dots, y_I$, where y_i is an observation of Y_i , the goal is to estimate $\mathbf{x} \triangleq [x_1 \ x_2 \ \dots \ x_J]^T$. In this way, an estimate for the number of photons emitted in each voxel is obtained. Throughout the remainder of this dissertation, $\mathbf{x}$ will be referred to as the *emission intensity*.

Shepp and Vardi used the expectation maximization algorithm [16] to compute a ML estimate of the emission intensity. This algorithm, which is referred to as the expectation maximization maximum likelihood algorithm, is briefly discussed in the Appendix.

In the next section, we discuss sources of errors in PET.

2.3 Errors in Positron Emission Tomography

In reality, PET data are corrupted by errors. In this section, we go through most of the important sources of error. Of all the errors, the one that has the most effect on image quality is attenuation [23]. Since we focus on developing new algorithms to correct attenuation, we provide an in depth discussion of attenuation.

2.3.1 Background on Attenuation

Attenuation is the main error source in PET emission image reconstruction [34]. The 511 keV photons produced by the annihilations are attenuated by tissue, bone, and air. Different mediums have different attenuation effects. Before going into the details of attenuation correction for PET, we introduce the physics behind attenuation.

The main sources of attenuation in PET are absorption and Compton scattering. Photons are rarely absorbed because they carry 511 keV of energy. Hence,

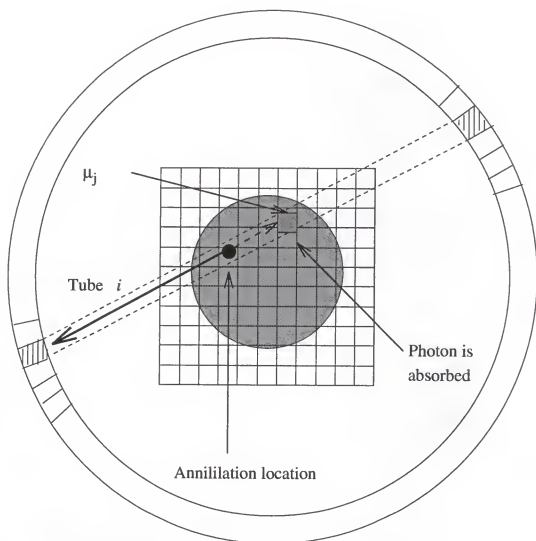


Figure 2.3. Attenuation due to absorption

attenuation due to absorption is negligible. Fig. 2.3 is a depiction of photon absorption. Compton scattering occurs when the path of the photon is deflected by an outer shell electron [37]. Photons in PET are more likely to undergo Compton scattering than absorption. Most of the photons that undergo Compton scattering are not detected. Fig. 2.4 shows a photon undergoing Compton scattering. The total effect of photon absorption and Compton scattering is referred to as *attenuation*.

The *survival probability along a line* L , α , is the probability that a photon is not attenuated along that line. It can be shown that the survival probability is equal to

$$\alpha = e^{-\int_L \mu dl} , \quad (2.3)$$

where μ is the attenuation density [29].

Since eq.(2.3) is a fundamental equation in attenuation, we provide an explanation of it. Consider Fig. 2.5, which shows a line source emitting photons toward an object with attenuation density μ . We assume that N photons incident on a point within the object travel a short distance, Δl , and only $N + \Delta N$ photons survive. Obviously, ΔN is a negative number. We may use the following equation to describe the above process:

$$\frac{\Delta N}{N} \frac{1}{\Delta l} = -\mu . \quad (2.4)$$

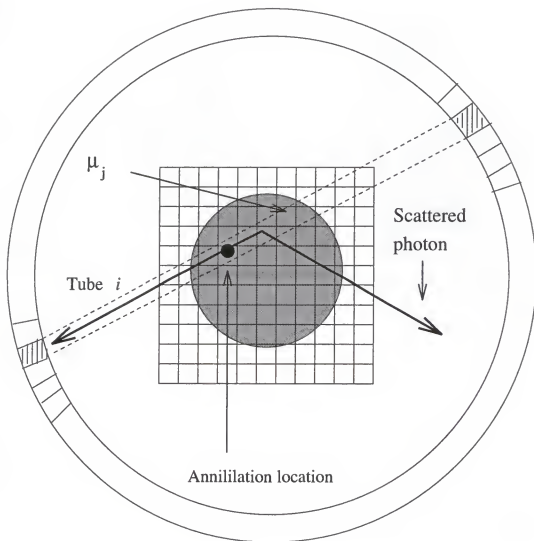


Figure 2.4. Attenuation due to scattering

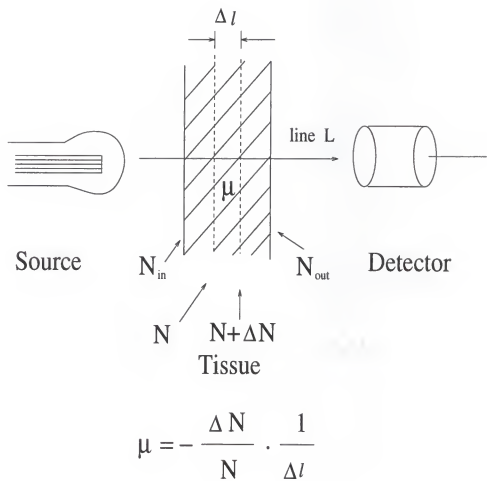


Figure 2.5. Basic concept of attenuation

As Δl and ΔN go to zero, we get the differential equation

$$\frac{1}{N} \frac{dN}{dl} = -\mu , \quad (2.5)$$

which can be solved by integrating along the line L . Doing so, we have that

$$\int_{N_{in}}^{N_{out}} \frac{dN}{N} = - \int_L \mu dl , \quad (2.6)$$

where N_{in} is the number of photons that go into the object and N_{out} is the number of photons that come out of the object. From the above equation, we get

$$\ln N_{out} - \ln N_{in} = - \int_L \mu dl . \quad (2.7)$$

It follows from eq. (2.7) that

$$\frac{N_{out}}{N_{in}} = e^{-\int_L \mu dl} . \quad (2.8)$$

Finally, eq. (2.3) follows by noting that the left side of (2.8) is the probability that a photon along the line L is not attenuated. In the next several sections, we discuss some other errors in PET.

2.3.2 Accidental Coincidences

If two photons from different annihilations are registered as a coincidence by a tube, then an error occurs. This kind of error is referred to as an *accidental coincidence* [22]. Fig. 2.6, shows an example of an accident coincidence. Two annihilations happen inside the ROI. However, in both annihilations, a photon flies out of the detector ring. The remaining photons are detected by a tube within the coincidence window and incorrectly recorded as a coincidence.

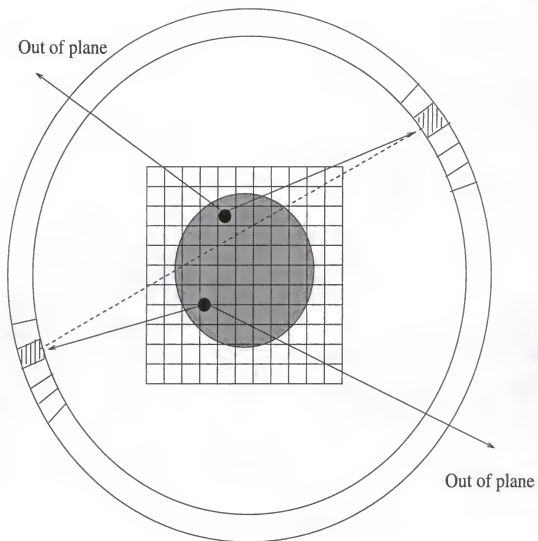


Figure 2.6. Accidental coincidence in PET

The accidental coincidence rate is proportional to the concentration of the radionuclide in the ROI. Usually, the accidental coincidences are corrected by subtracting an estimate of them from the observed photon counts. Accidental coincidences are estimated either by using an estimate of the single events to compute them or using a delayed coincidence circuitry to measure them [22]. This subtraction method may produce negative counts in the corrected data, which means that it is no longer Poisson. Consequently, several methods have been proposed to resolve this problem [2, 28, 41]. A discussion can be found in Anderson et al. [4] and Ollinger et al. [37]. In the next section, another error source, *scatter*, is reviewed.

2.3.3 Scatter

In a scattered event, one or both of the 511 keV photons created in an annihilation are scattered but they still intersect a detector ring. As a result, the annihilation event is registered by the wrong tube. An example of an error due to scatter is shown in Fig. 2.7.

Since photons lose energy after they are scattered, it is very easy to distinguish them from unscattered photons by measuring the energy they pass to the detector crystals [8]. This technique can be used to correct the scattered events by setting a threshold to reject photons with energy sufficiently less than 511 keV. Scatter between different slices in whole-body PET is minimized by the septa (see Section 2.1).

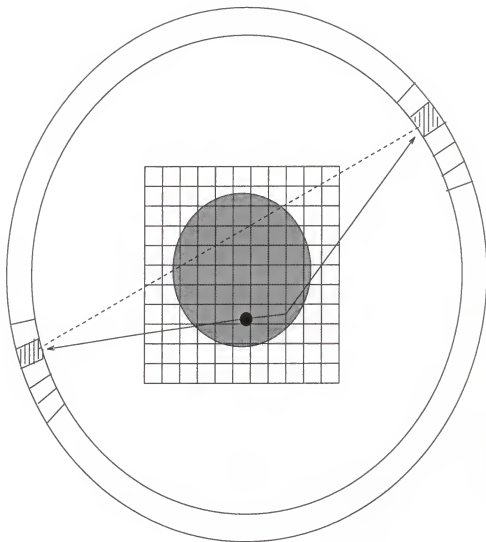


Figure 2.7. Scatter in PET

2.3.4 Other Errors

In reality, positrons travel a short distance (3-4 mm) before annihilating with an electron and photons shoot off at an angle less than 180° . Also, photons can penetrate the crystal they hit and leak energy to a neighboring tube [26]. Another type of error, called detector inefficiency, occurs when a detector fails to detect an incident photon [17]. Fortunately, most of the time, these errors are small and usually can be ignored or corrected.

In order to correct for attenuation, certain scans called blank scans and transmission scans are used to estimate the survival probability along each tube. In the next section, we provide a brief discussion of blank scans and transmission scans.

2.4 Transmission Tomography in PET

In order to correct for attenuation, a blank scan and transmission scan are performed. For the blank scan, a scan is done without a subject. The external photon source, as seen in Fig. 2.8, rotates along the interior of the detector ring. Let b_i denote the number of observed coincidences in tube i during the blank scan, $i = 1, 2, \dots, I$. The blank scan lasts about an hour to more than 2 hours. It is performed at the beginning of every day.

After positioning the subject in the scanner, a scan is performed, which is referred to as a transmission scan. Like the blank scan, the transmission scan uses a rotating external source of photons (see Fig. 2.9). The photon counts collected in a transmission scan are the ones that survive the attenuation effect of the ROI.

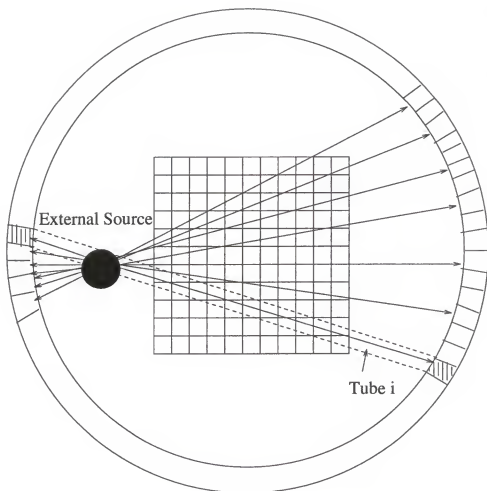


Figure 2.8. Blank scan

Let r_i denote the number of observed coincidences during the transmission scan for tube i , $i = 1, 2, \dots, I$. A transmission scan needs to be performed each time a new patient is put in the PET scanner. The duration of a transmission scan ranges from about 2 to 25 minutes. For the safety and comfort of the patient, the transmission scans are kept as short as possible. (patient should not be exposed to the radioactive source too long).

Intuitively, it is reasonable to estimate the survival probability by taking the ratio of the transmission scan count per unit time and the blank scan count per unit time. Hence, an estimate of the survival probability in tube i , $\hat{\alpha}_i$, is

$$\hat{\alpha}_i \triangleq \frac{r_i(\tau_b)}{b_i}, \quad (2.9)$$

where τ_b and τ_r are the durations of the blank scan and the transmission scan, respectively. The data can then be corrected for attenuation by dividing the data by the estimated survival probabilities (i.e., $\frac{y_i}{\alpha_i}$). This approach is simple and intuitively appealing, but it does not work well if the transmission scan is too short. One way to resolve that problem is to modify the Poisson model instead of directly correcting the data. In next section, we introduce the modified Poisson model.

2.5 Modified Poisson Model

In this section, we discuss an extension of the Poisson model for the case of attenuation errors only [28]. Before discussing this model, we introduce the concept of *thinning* a Poisson process.

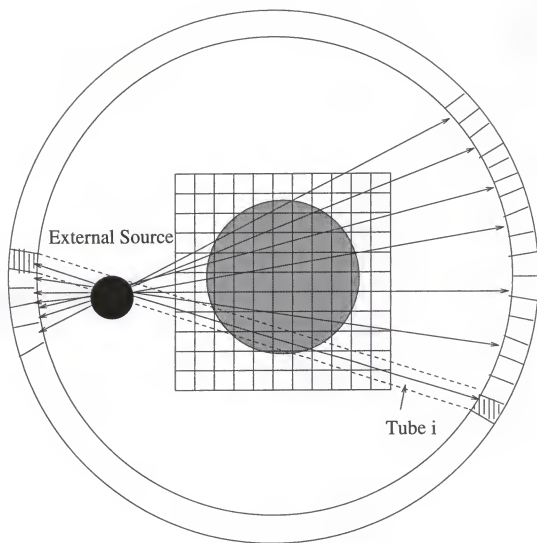


Figure 2.9. Transmission scan

Result 1: Let N be a Poisson random variable with mean x . Suppose a random variable X is created by thinning N with probability p . Then X is Poisson with mean px .

Proof:

$$\begin{aligned}
 P(X = k) &= \sum_{m=k}^{\infty} P(X = k|N = m)P(N = m) \\
 &= \sum_{m=k}^{\infty} \binom{m}{k} p^k (1-p)^{m-k} P(N = m) \\
 &= \sum_{m=k}^{\infty} \frac{m!}{k!(m-k)!} p^k (1-p)^{m-k} \frac{e^{-x} x^m}{m!} \\
 &= \frac{e^{-x} p^k}{k!} \sum_{m=k}^{\infty} \frac{(1-p)^{m-k} x^m}{(m-k)!}
 \end{aligned}$$

Replacing $m - k$ with n , yields

$$\begin{aligned}
 P(X = k) &= \frac{e^{-x} p^k}{k!} \sum_{n=0}^{\infty} \frac{(1-p)^n x^{n+k}}{n!} \\
 &= \frac{e^{-x} (xp)^k}{k!} \sum_{n=0}^{\infty} \frac{((1-p)x)^n}{n!} \\
 &= \frac{e^{-x} (xp)^k}{k!} e^{(1-p)x} \\
 &= \frac{e^{-xp} (xp)^k}{k!},
 \end{aligned}$$

which shows that X is a Poisson random variable with mean px .

We can apply Result 1 to model the effect of attenuation in PET (see also [41]). Let μ_j be the attenuation density within the j^{th} voxel, where it is assumed that the attenuation density within each voxel is constant. Let $\mathbf{L}$ be an $I \times J$ matrix whose $(i, j)^{\text{th}}$ element, L_{ij} , is the intersection length of the i^{th} tube and

the j^{th} voxel. Then, it follows from eq.(2.3) that the probability that a photon pair is detected by tube i is approximately equal to

$$\alpha_i \triangleq e^{-(\mathbf{L}\boldsymbol{\mu})_i}, \quad (2.10)$$

where $(\mathbf{L}\boldsymbol{\mu})_i = \sum_{j=1}^J L_{ij}\mu_j$, $i = 1, 2, \dots, I$. Because of attenuation, the data in tube i , Y_i , is created by thinning the error free data in tube i by the survival probability α_i . By Result 1, it follows that Y_i is Poisson with unknown mean

$$E[Y_i] = \alpha_i(\mathbf{P}\mathbf{x})_i. \quad (2.11)$$

With this modified Poisson model, several statistical reconstruction algorithms have been proposed.

2.6 Existing Attenuation Correction Methods

In this section, we review existing attenuation correction methods including those based on the modified Poisson model.

2.6.1 Standard Correction Method

The standard way to compensate for the attenuation is to divide the emission data by the estimate of the survival probabilities. Specifically, the *corrected data* for the i^{th} tube, $\hat{y}_i$, is given by

$$\hat{y}_i = \frac{y_i}{\hat{\alpha}_i}, i = 1, 2, \dots, I, \quad (2.12)$$

where $\hat{\alpha}_i$ is given by eq. (2.9).

This method is easy to implement and works fairly well for long transmission scans (20-25 minutes), for short transmission scans (less than 10 minutes), it produces noisy emission images. The conventional way this problem is addressed is to smooth the transmission sinogram. Smoothing reduces the noise, but it also lessens the quantitative accuracy of the images [34].

2.6.2 Reprojection Methods

Given the blank scan data and the transmission scan data, an estimate of the attenuation density is obtained [36, 41]. Then, the estimate, $\hat{\mu}$, is “reprojected” to obtain an estimate of the survival probabilities:

$$\hat{\alpha}_i = e^{-\sum_{j=1}^J L_{ij} \hat{\mu}_j}, i = 1, 2, \dots, I. \quad (2.13)$$

The estimated survival probabilities are used to correct the data or modify the probability matrix, P . In addition to improving the accuracy of the estimated survival probabilities, the transmission images provide information that can be used to position patients, estimate scattering errors, and to provide anatomical landmarks that cannot be seen in emission images [36].

The reprojection method provides a better estimate of the survival probabilities. However, the counting noise from the transmission image introduces additional error into the emission reconstruction. In regions such as the thorax, where the attenuation medium is heterogeneous, this problem cannot be resolved by

simply smoothing the estimated survival probabilities because it introduces bias [13]. Since reprojection methods estimate the attenuation density, they are more computationally demanding than the standard correction method. In the next section, we discuss methods that simultaneously estimate the attenuation density for survival probabilities and the emission intensity.

2.6.3 Simultaneous Estimation Methods

In [41], Politte and Snyder proposed constrained maximum likelihood reconstruction algorithms by modifying the probability matrix under the assumption of known survival probabilities. Their methods are not practical since the survival probabilities must be estimated. The transmission data provides noisy estimate of the survival probabilities because the count is pretty low in real applications. Since the emission data are more reliable than the transmission data, in the sense of having higher data counts, simultaneous estimation methods may provide a more accurate estimate of the emission intensity.

In [11], a simultaneous estimation method was proposed to estimate the attenuation density and the emission intensities for SPECT using the Cyclic Subgradient Projection (CSP) algorithm. After the Poisson model was proposed, Fessler, Clinthorne and Rogers proposed a joint maximum likelihood method that estimates the emission intensity and survival probabilities [13, 18]. Lu proposed a MAP algorithm to estimate the emission intensity and the attenuation density for SPECT [32]. However, prior information about the attenuation medium must be known.

To simultaneously estimate the attenuation density and the emission intensity, we propose a new method. In the next chapter, we discuss this proposed method.

CHAPTER 3

MAXIMUM LIKELIHOOD METHOD

In this chapter, we present an attenuation correction method that jointly estimates the attenuation density and emission intensity using a maximum likelihood (ML) method. Other ML methods have been proposed [13, 18], but they have the disadvantage of requiring more unknowns than data points. By contrast, the proposed method has fewer unknowns than data points for typical scanners. Specifically, it estimates $2J$ unknowns from I data points, where J and I are the number of the voxels and the number of the tubes, respectively. A common choice for the number of voxels is $J = 16384$ (i.e., $J = 128 \times 128$) and, for the Siemens-CTI ECAT EXACT 921 PET scanner, the number of the tubes is $I = 73536$.

3.1 Maximum Likelihood Estimator

As discussed in Section 2.2, the emission data for the i^{th} tube, y_i , is assumed to be an observation of a random variable, Y_i , where Y_i is Poisson with mean $(\mathbf{P}\mathbf{x})_i e^{-(\mathbf{L}\boldsymbol{\mu})_i}$ (recall, $(\mathbf{P}\mathbf{x})_i = \sum_{j=1}^J x_j P_{ij}$ and $(\mathbf{L}\boldsymbol{\mu})_i = \sum_{j=1}^J \mu_j L_{ij}$). The emission intensity, $\mathbf{x}$, and attenuation density, $\boldsymbol{\mu}$, are assumed to be deterministic but unknown. *Given the emission data, $y_1, y_2, \dots, y_I$, blank scan data, $b_1, b_2, \dots, b_I$, and transmission scan data, $r_1, r_2, \dots, r_I$, the goal is to estimate the emission intensity and attenuation density.*

It is well known that in many estimation problems ML estimators are consistent and asymptotically unbiased [44]. Thus, we propose to estimate the unknown parameters using a ML method. In other words, we estimate the emission intensity and attenuation density by maximizing the *log likelihood function*, $f(\mathbf{x}, \boldsymbol{\mu})$:

$$[\mathbf{x}^* \ \boldsymbol{\mu}^*] \triangleq \arg \max_{\mathbf{x}, \boldsymbol{\mu} \geq \mathbf{0}} f(\mathbf{x}, \boldsymbol{\mu}),$$

where $f(\mathbf{x}, \boldsymbol{\mu}) \triangleq \log P[Y_1 = y_1, Y_2 = y_2, \dots, Y_I = y_I | \mathbf{x}, \boldsymbol{\mu}]$, and $\mathbf{x}^*$ and $\boldsymbol{\mu}^*$ are ML estimates of $\mathbf{x}$ and $\boldsymbol{\mu}$, respectively. The notation $\mathbf{x} \geq \mathbf{0}$ means that all of the elements of $\mathbf{x}$ are nonnegative. Under the model assumptions, the log likelihood function is given by

$$f(\mathbf{x}, \boldsymbol{\mu}) = \log \prod_{i=1}^I P[Y_i = y_i | \mathbf{x}, \boldsymbol{\mu}] \quad (3.1)$$

$$= \log \prod_{i=1}^I \frac{e^{-[(P\mathbf{x})_i e^{-(L\boldsymbol{\mu})_i}]} [(P\mathbf{x})_i e^{-(L\boldsymbol{\mu})_i}]^{y_i}}{y_i!} \quad (3.2)$$

$$= \sum_{i=1}^I [- (P\mathbf{x})_i e^{-(L\boldsymbol{\mu})_i} + y_i \log(P\mathbf{x})_i - y_i (L\boldsymbol{\mu})_i - \log(y_i!)] . \quad (3.3)$$

Eq. (3.1) follows from the assumption that the data is independent. Note, since the last term in eq. (3.3) does not contain $\mathbf{x}$ or $\boldsymbol{\mu}$, it can be ignored in the maximization procedure. Thus, the above optimization problem is equivalent to the following one:

$$(\text{OP}) \quad [\mathbf{x}^* \ \boldsymbol{\mu}^*] \triangleq \arg \max_{\mathbf{x}, \boldsymbol{\mu} \geq \mathbf{0}} \phi(\mathbf{x}, \boldsymbol{\mu}),$$

where

$$\phi(\mathbf{x}, \boldsymbol{\mu}) = \sum_{i=1}^I [- (P\mathbf{x})_i e^{-(L\boldsymbol{\mu})_i} + y_i \log(P\mathbf{x})_i - y_i (L\boldsymbol{\mu})_i] . \quad (3.4)$$

The function $\phi(\mathbf{x}, \boldsymbol{\mu})$ will be referred to as the log likelihood function for the remainder of this dissertation.

The problem (**OP**) is a difficult constrained optimization problem that must be solved in order to obtain the ML estimate of the attenuation density and the emission intensity. In the next section, we discuss some properties of the log likelihood function before presenting our method for solving (**OP**).

3.2 Concavity of The Log Likelihood Function

Unfortunately, the log likelihood function, $\phi(\mathbf{x}, \boldsymbol{\mu})$, is not concave over the feasible region, $S_{\mathbf{x}, \boldsymbol{\mu}} \triangleq \{(\mathbf{x}, \boldsymbol{\mu}) | \mathbf{x} \geq 0, \boldsymbol{\mu} \geq 0\}$. However, for a fixed nonzero vector $\mathbf{z}_o$, $\phi(\mathbf{x}, \mathbf{z}_o)$ and $\phi(\mathbf{z}_o, \boldsymbol{\mu})$ are concave over the sets $S_{\mathbf{x}} \triangleq \{\mathbf{x} | \mathbf{x} \geq 0\}$ and $S_{\boldsymbol{\mu}} \triangleq \{\boldsymbol{\mu} | \boldsymbol{\mu} \geq 0\}$, respectively. These results are proved below.

Result 2: Let $\mathbf{z}_o$ be a nonzero $J \times 1$ vector. Then, $\phi(\mathbf{x}, \mathbf{z}_o)$ is concave over $S_{\mathbf{x}}$.

Proof:

Our proof is based on the well known fact that a function is concave if its Hessian is negative semidefinite [6]. Consider $\phi(\mathbf{x}, \mathbf{z}_o)$, where $\mathbf{z}_o \geq 0$ is a fixed $J \times 1$ vector. It follows from eq. (3.4) that $\phi(\mathbf{x}, \mathbf{z}_o)$ is given by

$$\phi(\mathbf{x}, \mathbf{z}_o) = \sum_{i=1}^I [-(\mathbf{P}\mathbf{x})_i e^{-(\mathbf{L}\mathbf{z}_o)_i} + y_i \log(\mathbf{P}\mathbf{x})_i - y_i(\mathbf{L}\mathbf{z}_o)_i],$$

and its first order partial derivative with respect to x_j equals

$$\frac{\partial \phi(\mathbf{x}, \mathbf{z}_o)}{\partial x_j} = \sum_{i=1}^I \left[\frac{y_i P_{ij}}{(\mathbf{P}\mathbf{x})_i} - e^{-(\mathbf{L}\mathbf{z}_o)_i} P_{ij} \right]. \quad (3.5)$$

The Hessian of $\phi(\mathbf{x}, \mathbf{z}_o)$, which we denote by $\mathbf{H}(\mathbf{x})$, is a $J \times J$ matrix whose $(j, k)^{\text{th}}$ element is given by

$$\mathbf{H}(\mathbf{x})_{jk} \triangleq \frac{\partial^2 \phi(\mathbf{x}, \mathbf{z}_o)}{\partial x_j \partial x_k} \quad (3.6)$$

$$= \sum_{i=1}^I -\frac{y_i P_{ij} P_{ik}}{(P\mathbf{x})_i^2}, \quad j, k = 1, 2, \dots, J. \quad (3.7)$$

Consider the scalar $\mathbf{m}^T \mathbf{H}(\mathbf{x}) \mathbf{m}$, where $\mathbf{m}$ and $\mathbf{x}$ are arbitrary nonzero vectors:

$$\mathbf{m}^T \mathbf{H}(\mathbf{x}) \mathbf{m} = - \sum_{k=1}^J \sum_{j=1}^J \sum_{i=1}^I \frac{y_i P_{ij} m_j P_{ik} m_k}{(P\mathbf{x})_i^2} \quad (3.8)$$

$$= \sum_{i=1}^I -\frac{y_i (P\mathbf{m})_i^2}{(P\mathbf{x})_i^2}. \quad (3.9)$$

Since for all i , $y_i \geq 0$, $(P\mathbf{m})_i^2 \geq 0$, and $(P\mathbf{x})_i \geq 0$, it follows that $\mathbf{m}^T \mathbf{H}(\mathbf{x}) \mathbf{m} \leq 0$, which means that the Hessian is negative semidefinite. Thus, $\phi(\mathbf{x}, \mathbf{z}_o)$ is concave over $S_{\mathbf{x}}$.

Result 3: Let $\mathbf{z}_o$ be a nonzero $J \times 1$ vector. Then, $\phi(\mathbf{z}_o, \boldsymbol{\mu})$ is concave over the set $S_{\boldsymbol{\mu}}$.

Proof:

Similar to the proof for Result 2, we need to prove that the Hessian of $\phi(\mathbf{z}_o, \boldsymbol{\mu})$ is negative semidefinite for $\mathbf{z}_o$, a nonzero fixed $J \times 1$ vector. From eq. (3.4), it follows that $\phi(\mathbf{z}_o, \boldsymbol{\mu})$ is given by

$$\phi(\mathbf{z}_o, \boldsymbol{\mu}) = \sum_{i=1}^I [- (P\mathbf{z}_o)_i e^{-(L\boldsymbol{\mu})_i} + y_i \log(P\mathbf{z}_o)_i - y_i (L\boldsymbol{\mu})_i],$$

and its first order partial derivative with respect to μ_j equals

$$\frac{\partial}{\partial \mu_j} \phi(\mathbf{z}_o, \boldsymbol{\mu}) = \sum_{i=1}^I (P\mathbf{z}_o)_i e^{-(L\boldsymbol{\mu})_i} L_{ij} - \sum_{i=1}^I y_i L_{ij}. \quad (3.10)$$

The Hessian of $\phi(\mathbf{z}_o, \boldsymbol{\mu})$, which we denote by $\mathbf{H}(\boldsymbol{\mu})$, is a $J \times J$ matrix whose $(j, k)^{\text{th}}$ element is given by

$$\mathbf{H}(\boldsymbol{\mu})_{jk} = \frac{\partial^2 \phi(\mathbf{z}_o, \boldsymbol{\mu})}{\partial \mu_j \partial \mu_k} \quad (3.11)$$

$$= - \sum_{i=1}^I (P\mathbf{z}_o)_i L_{ij} L_{ik} e^{-(L\boldsymbol{\mu})_i}, \quad j, k = 1, 2, \dots, J. \quad (3.12)$$

Consider the scalar $\mathbf{m}^T \mathbf{H}(\boldsymbol{\mu}) \mathbf{m}$, where $\mathbf{m}$ and $\boldsymbol{\mu}$ are arbitrary nonzero vectors:

$$\mathbf{m}^T \mathbf{H}(\boldsymbol{\mu}) \mathbf{m} = - \sum_{k=1}^J \sum_{j=1}^J \sum_{i=1}^I (P\mathbf{z}_o)_i L_{ij} m_j L_{ik} m_k e^{-(L\boldsymbol{\mu})_i} \quad (3.13)$$

$$= - \sum_{i=1}^I (P\mathbf{z}_o)_i (L\mathbf{m})_i^2 e^{-(L\boldsymbol{\mu})_i}. \quad (3.14)$$

For all i , $(P\mathbf{z}_o)_i \geq 0$, $e^{-(L\boldsymbol{\mu})_i} > 0$, and $(L\mathbf{m})_i^2 \geq 0$, hence it follows that $\mathbf{m}^T \mathbf{H}(\boldsymbol{\mu}) \mathbf{m} \leq 0$, which means that the Hessian is negative semidefinite. Thus, $\phi(\mathbf{z}_o, \boldsymbol{\mu})$ is concave over $S_{\boldsymbol{\mu}}$.

3.2.1 Example to Illustrate Concavity of the Log Likelihood Function

To get a sense of the “shape” of the log likelihood function, we consider the single voxel case. For this case, the log likelihood function becomes

$$\phi(x, \mu) = -pxe^{-l\mu} + y \log(px) - y l \mu. \quad (3.15)$$

It is straightforward to show that the Hessian of $\phi(x, \mu)$, which we denote by $\mathbf{H}$, is given by

$$\mathbf{H} = \begin{bmatrix} -\frac{y}{x^2} & ple^{-l\mu} \\ ple^{-l\mu} & -pxl^2e^{-l\mu} \end{bmatrix}.$$

Consider the scalar $\mathbf{m}^T \mathbf{H} \mathbf{m}$, where $\mathbf{m}$ is an arbitrary nonzero vector:

$$\mathbf{m}^T \mathbf{H} \mathbf{m} = -\frac{y}{x^2} m_1^2 - p x^l e^{-l\mu} m_2^2 + 2p l e^{-l\mu} m_1 m_2. \quad (3.16)$$

From eq. (3.16), it can be seen that there is no way to guarantee that $\mathbf{m}^T \mathbf{H} \mathbf{m}$ is less than or equal to zero. For $p = 1$, $l = 1$, $x = 40$, $\mu = 0.049$, $y = 2$, $m_1 = 0.2167$ and $m_2 = 0.01$, the log likelihood function is not concave (i.e., $\mathbf{m}^T \mathbf{H} \mathbf{m} > 0$).

3.3 Optimization Procedure

We exploit the concavity results discussed in last section and propose the following optimization procedure to obtain the ML estimates (i.e., solve (OP)):

(Step 1) Given $\boldsymbol{\mu}^{k-1}$ and $\mathbf{x}^{k-1}$, determine $\mathbf{x}^k$ by maximizing $\phi(\mathbf{x}, \boldsymbol{\mu}^{k-1})$ over $S_{\mathbf{x}}$.

In other words,

$$(P1) \quad \mathbf{x}^k \triangleq \arg \max_{\mathbf{x} \geq \mathbf{0}} \phi(\mathbf{x}, \boldsymbol{\mu}^{k-1}).$$

(Step 2) Given $\boldsymbol{\mu}^{k-1}$ and $\mathbf{x}^k$, determine $\boldsymbol{\mu}^k$ by maximizing $\phi(\mathbf{x}^k, \boldsymbol{\mu})$ over $S_{\boldsymbol{\mu}}$. That is,

$$(P2) \quad \boldsymbol{\mu}^k \triangleq \max_{\boldsymbol{\mu} \geq \mathbf{0}} \phi(\mathbf{x}^k, \boldsymbol{\mu}).$$

(Step 3) Iterate between Step 1 and Step 2.

Step 1 and Step 2 are referred to as the *x-step* and the *μ -step*, respectively. The vectors $\mathbf{x}^k$ and $\boldsymbol{\mu}^k$ are the k^{th} estimate of $\mathbf{x}$ and $\boldsymbol{\mu}$, respectively, where an iteration consists of both steps 1 and 2. Unfortunately, closed form solutions for $\mathbf{x}^k$ and $\boldsymbol{\mu}^k$ are not available, which means they must be determined using iterative

algorithms. In the next two sections, we develop algorithms for obtaining $\mathbf{x}^k$ and $\boldsymbol{\mu}^k$.

3.3.1 x -step

Given $\boldsymbol{\mu}^{k-1} \geq 0$, we know that $\phi(\mathbf{x}, \boldsymbol{\mu}^{k-1})$ is concave over $S_{\mathbf{x}}$ from Result 2. Under the conditions in problem (P1), $\hat{\mathbf{x}}$ is a solution to (P1) if and only if the Kuhn-Tucker conditions [54] are satisfied:

$$\begin{aligned} \frac{\partial \phi(\mathbf{x}, \boldsymbol{\mu}^{k-1})}{\partial x_j} \Big|_{\mathbf{x}=\hat{\mathbf{x}}} &= 0 \quad \text{if } x_j \neq 0, \quad j = 1, 2, \dots, J, \\ \frac{\partial \phi(\mathbf{x}, \boldsymbol{\mu}^{k-1})}{\partial x_j} \Big|_{\mathbf{x}=\hat{\mathbf{x}}} &\leq 0 \quad \text{if } x_j = 0, \quad j = 1, 2, \dots, J. \end{aligned}$$

We can rewrite the above two Kuhn-Tucker conditions as

$$(C1) \quad \sum_{i=1}^I \frac{y_i P_{ij}}{(\mathbf{P}\hat{\mathbf{x}})_i} = \sum_{i=1}^I e^{-(\mathbf{L}\boldsymbol{\mu}^{k-1})_i} P_{ij} \quad \text{if } x_j \neq 0, \quad j = 1, 2, \dots, J,$$

$$(C2) \quad \sum_{i=1}^I \frac{y_i P_{ij}}{(\mathbf{P}\hat{\mathbf{x}})_i} \leq \sum_{i=1}^I e^{-(\mathbf{L}\boldsymbol{\mu}^{k-1})_i} P_{ij} \quad \text{if } x_j = 0, \quad j = 1, 2, \dots, J.$$

The first condition (C1) suggests the following fixed point iteration for solving (P1):

$$(\mathbf{x}^k)_j^{m+1} = (\mathbf{x}^k)_j^m \frac{\sum_{i=1}^I \frac{y_i P_{ij}}{(\mathbf{P}(\mathbf{x}^k)_j^m)_i}}{\sum_{i=1}^I e^{-(\mathbf{L}\boldsymbol{\mu}^{k-1})_i} P_{ij}}, \quad j = 1, 2, \dots, J, \quad (3.17)$$

where $(\mathbf{x}^k)_j^m$ is the m^{th} estimate of the j^{th} voxel of $\mathbf{x}^k$ and $(\mathbf{x}^k)_j^0 = (\mathbf{x}^{k-1})_j$ for all j . Another possible iteration is

$$(\mathbf{x}^k)_j^{m+1} = (\mathbf{x}^k)_j^m \frac{\sum_{i=1}^I e^{-(\mathbf{L}\boldsymbol{\mu}^{k-1})_i} P_{ij}}{\sum_{i=1}^I \frac{y_i P_{ij}}{(\mathbf{P}(\mathbf{x}^k)_j^m)_i}}, \quad j = 1, 2, \dots, J. \quad (3.18)$$

However, in our simulations, this iteration “blew up” (i.e., the iterates became unbounded). Consequently, we use the iteration in eq. (3.17) to estimate $\mathbf{x}^k$.

The logic behind the fixed point iteration in eq.(3.17) is discussed below. Suppose $(\mathbf{x}^k)_j^m$ converges to $(\mathbf{x}^k)_j^\infty \neq 0$, then from eq.(3.17) we have

$$(\mathbf{x}^k)_j^\infty = (\mathbf{x}^k)_j^\infty \frac{\sum_{i=1}^I \frac{y_i P_{ij}}{(\mathbf{P}(\mathbf{x}^k)^\infty)_i}}{\sum_{i=1}^I \alpha_i^{k-1} P_{ij}}, \quad (3.19)$$

which implies that condition **(C1)** is satisfied. In other words, we know that the fixed point iteration in eq.(3.17) will provide a solution satisfying **(C1)** if it converges to a positive vector. Additional motivation for the technique used to derive the algorithm in eq. (3.17) is that the EML algorithm [28, 46] and the ISRA algorithm [15] can be derived using it. *Applying the alternating projection method [10] to solve (P1) leads to the same iterative equation as eq. (3.17).* This iteration is guaranteed to converge by convergence results in Byrne's paper [10].

3.3.2 μ -step

From Result 3, we know that $\phi(\mathbf{x}^k, \boldsymbol{\mu})$ is concave over $S_{\boldsymbol{\mu}}$ for $\mathbf{x}^k \geq 0$. Thus, $\hat{\boldsymbol{\mu}}$ is a solution to **(P2)** if and only if the following Kuhn-Tucker conditions hold:

$$(C3) \quad \sum_{i=1}^I (\mathbf{P}\mathbf{x}^k)_i e^{-(L\hat{\boldsymbol{\mu}})_i} L_{ij} = \sum_{i=1}^I y_i L_{ij} \quad \text{if } \mu_j \neq 0, \quad j = 1, 2, \dots, J,$$

$$(C4) \quad \sum_{i=1}^I (\mathbf{P}\mathbf{x}^k)_i e^{-(L\hat{\boldsymbol{\mu}})_i} L_{ij} \leq \sum_{i=1}^I y_i L_{ij} \quad \text{if } \mu_j = 0, \quad j = 1, 2, \dots, J.$$

Using the same approach that leads to the iteration in eq. (3.17), we obtain the following fixed point iteration for solving problem **(P2)**:

$$(\boldsymbol{\mu}^k)_j^{m+1} = (\boldsymbol{\mu}^k)_j^m \frac{\sum_{i=1}^I e^{-(L(\boldsymbol{\mu}^k)^m)_i} (\mathbf{P}\mathbf{x}^k)_i L_{ij}}{\sum_{i=1}^I y_i L_{ij}}, \quad j = 1, 2, \dots, J, \quad (3.20)$$

where $(\boldsymbol{\mu}^k)_j^m$ is the m^{th} estimate of the j^{th} voxel of $\boldsymbol{\mu}^k$ and $(\boldsymbol{\mu}^k)_j^0 = (\boldsymbol{\mu}^{k-1})_j$ for all j . Another possible iterative equation is

$$(\boldsymbol{\mu}^k)_j^{m+1} = (\boldsymbol{\mu}^k)_j^m \frac{\sum_{i=1}^I y_i L_{ij}}{\sum_{i=1}^I e^{-(\mathbf{L}(\boldsymbol{\mu}^k)^m)_i} (\mathbf{P}\mathbf{x}^k)_i L_{ij}}, \quad j = 1, 2, \dots, J. \quad (3.21)$$

In our simulations, this iteration “blew up”. Consequently, we estimate $\boldsymbol{\mu}^k$ using the iteration in eq. (3.20).

In the next section, we investigate the behavior of the log likelihood function as a function of the iterates.

3.3.3 Monotonically Increasing Value of the Log Likelihood Function in x -step

From the log likelihood function given in eq.(3.4) and the iterative equation in eq.(3.17), we can prove that the log likelihood function increases monotonically with successive iteration in the x -step. Unfortunately, this result cannot be proven for the μ -step.

Result 5: Let $\mathbf{z}_o$ be a fixed nonzero $J \times 1$ vector. Then,

$$\phi((\mathbf{x}^k)^{m+1}, \mathbf{z}_o) - \phi((\mathbf{x}^k)^m, \mathbf{z}_o) \geq 0.$$

Proof:

From eq.(3.4), it is easy to see that

$$\begin{aligned} & \phi((\mathbf{x}^k)^{m+1}, \mathbf{z}_o) - \phi((\mathbf{x}^k)^m, \mathbf{z}_o) \\ &= \sum_{i=1}^I [-(\mathbf{P}(\mathbf{x}^k)^{m+1})_i + (\mathbf{P}(\mathbf{x}^k)^m)_i] \alpha_i + \sum_{i=1}^I y_i \log \frac{(\mathbf{P}(\mathbf{x}^k)^{m+1})_i}{(\mathbf{P}(\mathbf{x}^k)^m)_i}, \end{aligned}$$

where $\alpha_i = e^{-(\mathbf{L}\mathbf{z}_o)_i}$.

Hence, using the iterative equation in eq.(3.17), it follows that the second term of the above derivation can be written as

$$\begin{aligned}
\sum_{i=1}^I y_i \log \frac{(P(\mathbf{x}^k)^{m+1})_i}{(P(\mathbf{x}^k)^m)_i} &= \sum_{i=1}^I y_i \log \sum_{j=1}^J \frac{P_{ij}(\mathbf{x}^k)_j^{m+1}}{(P(\mathbf{x}^k)^m)_i} \\
&= \sum_{i=1}^I y_i \log \sum_{j=1}^J \left[\frac{P_{ij}}{(P(\mathbf{x}^k)^m)_i} (\mathbf{x}^k)_j^m \omega_j^k \right] \\
&= \sum_{i=1}^I y_i \log \sum_{j=1}^J \left[\frac{P_{ij}(\mathbf{x}^k)_j^m}{(P(\mathbf{x}^k)^m)_i} \omega_j^k \right],
\end{aligned}$$

where $\omega_j^k = \frac{\sum_{i=1}^I \frac{y_i P_{ij}}{(P(\mathbf{x}^k)^m)_i}}{\sum_{i=1}^I \alpha_i P_{ij}}.$

Let $\beta_{ij} = \frac{P_{ij}(\mathbf{x}^k)_j^m}{(P(\mathbf{x}^k)^m)_i}$, $\sum_{j=1}^J \beta_{ij} = 1$. Using the fact that the log function is concave, we have

$$\sum_{i=1}^I y_i \log \sum_{j=1}^J \beta_{ij} \omega_j^k \geq \sum_{i=1}^I y_i \sum_{j=1}^J \beta_{ij} \log \omega_j^k. \quad (3.22)$$

Multiplying the right side of eq.(3.22) by $\frac{(\sum_{i=1}^I \alpha_i P_{ij})}{(\sum_{i=1}^I \alpha_i P_{ij})}$, the value of right side of eq.(3.22) does not change since $\frac{(\sum_{i=1}^I \alpha_i P_{ij})}{(\sum_{i=1}^I \alpha_i P_{ij})} = 1$. Then, it follows that

$$\begin{aligned}
\sum_{i=1}^I y_i \sum_{j=1}^J \beta_{ij} \log \omega_j^k &= \sum_{i=1}^I y_i \left(\sum_{i=1}^I \alpha_i P_{ij} \right) \frac{\sum_{j=1}^J \beta_{ij} \log \omega_j^k}{\sum_{i=1}^I \alpha_i P_{ij}} \\
&= \sum_{j=1}^J x_j^k \left(\sum_{i=1}^I \alpha_i P_{ij} \right) \frac{\sum_{i=1}^I \frac{y_i P_{ij}}{(P(\mathbf{x}^k)^m)_i}}{\sum_{i=1}^I \alpha_i P_{ij}} \log \omega_j^k \\
&= \sum_{j=1}^J x_j^k \left(\sum_{i=1}^I \alpha_i P_{ij} \right) \omega_j^k \log \omega_j^k
\end{aligned}$$

$$\begin{aligned}
&\geq \sum_{j=1}^J x_j^k (\sum_{i=1}^I \alpha_i P_{ij})(\omega_j^k - 1) \\
&= \sum_{j=1}^J x_j^k \sum_{i=1}^I \frac{y_i P_{ij}}{(P(\mathbf{x}^k)^m)_i} - \sum_{i=1}^I \alpha_i \sum_{j=1}^J P_{ij} (\mathbf{x}^k)_j^m \\
&= \sum_{i=1}^I y_i - \sum_{i=1}^I \alpha_i (P(\mathbf{x}^k)^m)_i .
\end{aligned}$$

Since $\sum_{i=1}^I y_i \log \sum_{j=1}^J \beta_{ij} \omega_j^k \geq \sum_{i=1}^I y_i \sum_{j=1}^J \beta_{ij} \log \omega_j^k$, we have

$$\sum_{i=1}^I y_i \log \frac{(P(\mathbf{x}^k)^{m+1})_i}{(P(\mathbf{x}^k)^m)_i} \geq \sum_{i=1}^I y_i - \sum_{i=1}^I \alpha_i (P(\mathbf{x}^k)^m)_i . \quad (3.23)$$

Then, we get

$$\begin{aligned}
&\phi((\mathbf{x}^k)^{m+1}, \mathbf{z}_o) - \phi((\mathbf{x}^k)^m, \mathbf{z}_o) \\
&\geq \sum_{i=1}^I y_i - \sum_{i=1}^I [\alpha_i (P(\mathbf{x}^k)^m)_i + \alpha_i (P(\mathbf{x}^k)^m)_i - \alpha_i (P(\mathbf{x}^k)^{m+1})_i] \\
&= \sum_{i=1}^I y_i - \sum_{i=1}^I \alpha_i (P(\mathbf{x}^k)^{m+1})_i .
\end{aligned}$$

From eq.(3.4), we know that

$$\sum_{i=1}^I \alpha_i (P(\mathbf{x}^k)^{m+1})_i = \sum_{i=1}^I \frac{y_i (P(\mathbf{x}^k)^m)_i}{(P(\mathbf{x}^k)^m)_i} = \sum_{i=1}^I y_i . \quad (3.24)$$

From eq.(3.24), we obtain

$$\sum_{i=1}^I y_i - \sum_{i=1}^I \alpha_i (P(\mathbf{x}^k)^{m+1})_i = 0 \quad (3.25)$$

Thus, we get the desired result.

$$\phi((\mathbf{x}^k)^{m+1}, \mathbf{z}_o) - \phi((\mathbf{x}^k)^m, \mathbf{z}_o) \geq 0 .$$

In the next section, an interesting property of the ML estimator is presented.

3.3.4 Property of the ML Estimator

Result 4: Suppose there exists a solution $(\mathbf{x}^*, \boldsymbol{\mu}^*)$ to (OP). Then,

$$\frac{\sum_{i=1}^I \frac{y_i P_{ij}}{(\mathbf{P}\mathbf{x}^*)_i}}{\sum_{i=1}^I e^{-(\mathbf{L}\boldsymbol{\mu}^*)_i} P_{ij}} \leq 1, \quad (3.26)$$

$$\frac{\sum_{i=1}^I (\mathbf{P}\mathbf{x}^*)_i e^{-(\mathbf{L}\boldsymbol{\mu}^*)_i} L_{ij}}{\sum_{i=1}^I y_i L_{ij}} \leq 1, \quad j = 1, 2, \dots, J. \quad (3.27)$$

Proof:

Consider the log likelihood function

$$\phi(\mathbf{x}, \boldsymbol{\mu}) = \sum_{i=1}^I [-(\mathbf{P}\mathbf{x})_i e^{-(\mathbf{L}\boldsymbol{\mu})_i} + y_i \log(\mathbf{P}\mathbf{x})_i - y_i (\mathbf{L}\boldsymbol{\mu})_i].$$

Suppose that there exists an optimal solution $(\mathbf{x}^*, \boldsymbol{\mu}^*)$ and let t be a nonnegative scalar, and $\mathbf{x}$ and $\boldsymbol{\mu}$ be nonnegative vectors. Then, $\phi(\mathbf{x}^* + t\mathbf{x}, \boldsymbol{\mu}^* + t\boldsymbol{\mu}) \leq \phi(\mathbf{x}^*, \boldsymbol{\mu}^*)$. From the above relationship, we get

$$\begin{aligned} & \sum_{i=1}^I \{y_i \log[\frac{(\mathbf{P}\mathbf{x}^*)_i + t(\mathbf{P}\mathbf{x})_i}{(\mathbf{P}\mathbf{x}^*)_i}] - ty_i (\mathbf{L}\boldsymbol{\mu})_i \\ & - [(\mathbf{P}\mathbf{x}^*)_i + t(\mathbf{P}\mathbf{x})_i] e^{-[(\mathbf{L}\boldsymbol{\mu}^*)_i + t(\mathbf{L}\boldsymbol{\mu})_i]} + (\mathbf{P}\mathbf{x}^*)_i e^{-(\mathbf{L}\boldsymbol{\mu}^*)_i} \} \leq 0 \end{aligned}$$

Since $(\mathbf{P}\mathbf{x}^*)_i e^{-(\mathbf{L}\boldsymbol{\mu}^*)_i} \geq 0$ for all i , we have

$$\begin{aligned} & \sum_{i=1}^I \{y_i \log[\frac{(\mathbf{P}\mathbf{x}^*)_i + t(\mathbf{P}\mathbf{x})_i}{(\mathbf{P}\mathbf{x}^*)_i}] \\ & - ty_i (\mathbf{L}\boldsymbol{\mu})_i - [(\mathbf{P}\mathbf{x}^*)_i + t(\mathbf{P}\mathbf{x})_i] e^{-[(\mathbf{L}\boldsymbol{\mu}^*)_i + t(\mathbf{L}\boldsymbol{\mu})_i]} \} \leq 0 \quad (3.28) \end{aligned}$$

Dividing eq.(3.28) by t , we get

$$\sum_{i=1}^I \{ \frac{y_i}{t} \log[1 + \frac{(\mathbf{P}\mathbf{x})_i}{(\mathbf{P}\mathbf{x}^*)_i}] - y_i (\mathbf{L}\boldsymbol{\mu})_i - [\frac{(\mathbf{P}\mathbf{x}^*)_i}{t} + (\mathbf{P}\mathbf{x})_i] e^{-[(\mathbf{L}\boldsymbol{\mu}^*)_i + t(\mathbf{L}\boldsymbol{\mu})_i]} \} \leq 0. \quad (3.29)$$

Now letting $t \rightarrow 0$ and using the L'Hoptial's rule, we obtain

$$\sum_{i=1}^I \left\{ \frac{y_i(\mathbf{P}\mathbf{x})_i}{(\mathbf{P}\mathbf{x}^*)_i} - y_i(\mathbf{L}\boldsymbol{\mu})_i + (\mathbf{P}\mathbf{x})_i^* (\mathbf{L}\boldsymbol{\mu})_i e^{-(\mathbf{L}\boldsymbol{\mu}^*)_i} - (\mathbf{P}\mathbf{x})_i e^{-(\mathbf{L}\boldsymbol{\mu}^*)_i} \right\} \leq 0. \quad (3.30)$$

Since eq.(3.30) must hold for any $\boldsymbol{\mu} \geq 0$ and $\mathbf{x} \geq 0$, we consider the case where $\mathbf{x} = \mathbf{e}_j$ ($\mathbf{e}_j$ is a $J \times 1$ vector of zeros except for the j^{th} element which is a one) and $\boldsymbol{\mu} = 0$. For this case, eq. (3.30) becomes

$$\sum_{i=1}^I \left[\frac{y_i P_{ij}}{(\mathbf{P}\mathbf{x}^*)_i} - e^{-(\mathbf{L}\boldsymbol{\mu}^*)_i} P_{ij} \right] \leq 0, \quad j = 1, 2, \dots, J. \quad (3.31)$$

Similarly, for $\mathbf{x} = 0$ and $\boldsymbol{\mu} = \mathbf{e}_j$, eq. (3.30) yields

$$\sum_{i=1}^I [-y_i L_{ij} + (\mathbf{P}\mathbf{x}^*)_i e^{-(\mathbf{L}\boldsymbol{\mu}^*)_i} L_{ij}] \leq 0, \quad j = 1, 2, \dots, J. \quad (3.32)$$

Note, eq. (3.31) and (3.32) are only necessary conditions for $(\mathbf{x}^*, \boldsymbol{\mu}^*)$ to be a maximum of $\phi(\mathbf{x}, \boldsymbol{\mu})$ over the feasible region. Since $\mathbf{x}^*, \boldsymbol{\mu}^* \geq 0$, it follows from eq. (3.31) and eq. (3.32) that

$$\frac{\sum_{i=1}^I \frac{y_i P_{ij}}{(\mathbf{P}\mathbf{x}^*)_i}}{\sum_{i=1}^I e^{-(\mathbf{L}\boldsymbol{\mu}^*)_i} P_{ij}} \leq 1, \quad j = 1, 2, \dots, J, \quad (3.33)$$

$$\frac{\sum_{i=1}^I (\mathbf{P}\mathbf{x}^*)_i e^{-(\mathbf{L}\boldsymbol{\mu}^*)_i} L_{ij}}{\sum_{i=1}^I y_i L_{ij}} \leq 1, \quad j = 1, 2, \dots, J. \quad (3.34)$$

In the next chapter, we introduce a new least squares reprojection attenuation correction method.

CHAPTER 4

LEAST SQUARES REPROJECTION METHOD

In this chapter, we introduce a reprojection method, where the attenuation density is estimated using a least squares (LS) algorithm. The algorithm is an extension of one proposed by Anderson, et. al. [4] for X-ray computed tomography.

4.1 LS Algorithm for Estimating the Attenuation Density

As discussed in Section 2.4 and 2.5, let b_i denote the number of photons detected in tube i during the blank scan. It is assumed that b_i is an observation of a random variable, B_i , where B_i is Poisson with mean $U_i > 0$. It is also assumed that the number of photons detected in tube i during the transmission scan, r_i , is an observation of a random variable, R_i , where R_i is Poisson with mean $U_i \alpha_i(\frac{\tau}{\tau_b})$ (recall $\alpha_i \triangleq e^{-(\mathbf{L}\boldsymbol{\mu})_i}$). Given the observed blank scan data, $b_1, b_2, \dots, b_I$, and the observed transmission data, $r_1, r_2, \dots, r_I$, the goal is to estimate the attenuation density, $\boldsymbol{\mu}$.

It is straightforward to show that b_i and r_i are the ML estimates of U_i and $U_i \alpha_i(\frac{\tau}{\tau_b})$, respectively. Consequently, $b_i \approx U_i$ and $r_i \approx U_i \alpha_i(\frac{\tau}{\tau_b})$. These approximations lead to the following one: $\alpha_i \approx \frac{r_i}{b_i}(\frac{\tau_b}{\tau})$. Taking the logarithm on both sides of this relationship and multiplying the result by negative one, we get $(\mathbf{L}\boldsymbol{\mu})_i \approx d_i$, where $d_i = -\log(\frac{r_i}{b_i}(\frac{\tau_b}{\tau}))$. Exploiting this observation, we propose to estimate the attenuation density by minimizing the 2-norm distance between $\mathbf{d}$ and $(\mathbf{L}\boldsymbol{\mu})$:

$$(P3) \quad \boldsymbol{\mu}^* = \min_{\boldsymbol{\mu} \geq \mathbf{0}} \rho(\boldsymbol{\mu}) ,$$

where $\rho(\boldsymbol{\mu}) = \sum_{i=1}^I (d_i - (\mathbf{L}\boldsymbol{\mu})_i)^2$, $\boldsymbol{\mu}^*$ is the LS estimate of $\boldsymbol{\mu}$, and $\mathbf{d} = [d_1, d_2, \dots, d_I]$. It is straightforward to show that $\rho(\boldsymbol{\mu})$ is convex over $S_{\boldsymbol{\mu}}$.

A vector $\hat{\boldsymbol{\mu}}$ is a solution to (P3) if and only if it satisfies the following Kuhn-Tucker conditions:

$$(C5) \quad \sum_{i=1}^I \mathbf{L}_{ij}(d_i - (\mathbf{L}\hat{\boldsymbol{\mu}})_i) = 0 \quad \text{if } \mu_j \neq 0, \quad j = 1, 2, \dots, J,$$

$$(C6) \quad \sum_{i=1}^I -\mathbf{L}_{ij}(d_i - (\mathbf{L}\hat{\boldsymbol{\mu}})_i) \geq 0 \quad \text{if } \mu_j = 0, \quad j = 1, 2, \dots, J.$$

As before (see Chapter 3), the first condition (C5) motivates the following fixed point iteration:

$$\mu_j^{k+1} = \mu_j^k \frac{\sum_{i=1}^I d_i \mathbf{L}_{ij}}{\sum_{i=1}^I (\mathbf{L}\boldsymbol{\mu}^k)_i \mathbf{L}_{ij}}, \quad j = 1, 2, \dots, J, \quad (4.1)$$

where μ_j^k is the k^{th} estimate of μ_j . *This iteration has exactly the same form as the iterative image space reconstruction algorithm for PET [15]. Since it has been proven that the iterative image space reconstruction algorithm converges [40], the proposed LS algorithm converges as well.* In the next section, we discuss how the LS estimate of the attenuation density is used to correct for attenuation.

4.2 LS Reprojection Method

Given the blank scan data and the transmission scan data, we estimate the attenuation density using eq. (4.1). Let $\bar{\boldsymbol{\mu}}$ be the resulting estimate. Then, the survival probabilities are estimated by reprojecting $\bar{\boldsymbol{\mu}}$:

$$\bar{\alpha}_i = e^{-\sum_{j=1}^J L_{ij} \bar{\mu}_j}, \quad i = 1, 2, \dots, I. \quad (4.2)$$

Next, the estimated survival probabilities are used to create a modified probability matrix, $\bar{\mathbf{P}}$, where $\bar{P}_{ij} = \bar{\alpha}_i P_{ij}$. The emission intensity is then estimated by using

the EML algorithm with the modified probability matrix:

$$x_j^{k+1} = x_j^k \frac{\sum_{i=1}^I \frac{y_i P_{ij}}{(\mathbf{P}\mathbf{x}^k)_i}}{\sum_{i=1}^I \bar{P}_{ij}}, \quad j = 1, 2, \dots, J. \quad (4.3)$$

It is straightforward to show that this iteration is equivalent to

$$x_j^{k+1} = x_j^k \frac{\sum_{i=1}^I \frac{y_i P_{ij}}{(\mathbf{P}\mathbf{x}^k)_i}}{\sum_{i=1}^I \hat{\alpha}_i P_{ij}}, \quad j = 1, 2, \dots, J. \quad (4.4)$$

In the next chapter, simulations are used to compare the performance of the ML method, LS reprojection method, and EML algorithm with corrected data.

CHAPTER 5 SIMULATION

Using synthetic data and real data, we assess the proposed methods and compare them to the EML algorithm with corrected data. Dr. John Votaw, Associate Professor of Radiology at the Emory University Hospital provided the real data. This data was collected on the Siemens-CTI ECAT EXACT 921 PET scanner. The probabilities, P_{ij} , and line length, L_{ij} , were determined from the diameter of the detector ring, number of detectors, the size of ROI (the ROI is always a square centered in the middle of the detector ring), and the number of voxels. Specially, the probabilities are calculated using the angle-of-view method [46]. It should be noted that the probabilities and line lengths are calculated under the assumption that the detectors are contiguous. The number of detectors for the simulated scanner and the Siemens-CTI ECAT EXACT 921 scanner are 300 and 384, respectively. The computational expense of an iteration for the ML method, LS reprojection method, and the EML algorithm with corrected data are essentially the same. Consequently, the computational complexity of the algorithms can be compared by considering the total number of iterations required by each one.

5.1 Synthetic Data

For the synthetic data, we use a cardiac emission phantom (see Fig. 5.3 (a)), chest emission phantom (see Fig. 5.7 (a)), cardiac attenuation phantom (see Fig. 5.5 (a)), and chest attenuation phantom (see Fig. 5.8 (a)). All of the phantoms are of size 100×100 , and the voxel size for the cardiac phantoms and chest phantoms are 0.422 cm and 0.437 cm, respectively. The lungs, spine, and soft tissue region in the cardiac attenuation phantom have densities 0.025 cm^{-1} , 0.16 cm^{-1} , and 0.096 cm^{-1} , respectively. The low density regions (light color region) and the high density regions (dark color region) in the chest attenuation phantom have densities 0.035 cm^{-1} and 0.095 cm^{-1} , respectively. The diameter of the detector ring for the cardiac phantoms and chest phantoms is 59.68 cm and 61.8 cm, respectively. The ROI for the cardiac phantoms and chest phantoms is 42.2 cm and 43.7 cm, respectively. The number of tubes is $I = 44850$.

We generate the emission scan, transmission scan, and blank scan data in the following manner. The observed coincidence for the i^{th} tube, y_i , is the observation of a Poisson random variable with mean $(\mathbf{P}\mathbf{x})_i\alpha_i$ (recall $\alpha_i = e^{-(\mathbf{L}\boldsymbol{\mu})_i}$). The emission phantoms and attenuation phantoms specify $\mathbf{x}$ and $\boldsymbol{\mu}$, respectively. The observed count for the blank scan for the i^{th} tube, b_i , and the transmission scan for the i^{th} tube, r_i , are Poisson random variables with means U_i and $U_i\alpha_i(\frac{x}{\tau_b})$, respectively. We specify the total count of the transmission scan to be R . and use

$$U_i = \frac{R}{(\sum_{i=1}^I \alpha_i)(\frac{x}{\tau_b})I}, \quad i = 1, 2, \dots, I.$$

5.1.1 ML Method Implementation of Algorithms

The term *local iteration* refers to the iterations used to determine $\mathbf{x}^k$ and $\boldsymbol{\mu}^k$ in Step 1 (x -step) and Step 2 (μ -step), respectively (see (P1) and (P2) in Section 3.3). The term *global iteration* refers to a single execution of both the x -step and the μ -step. For the simulations using synthetic data, we run 8 local iterations for the x -step, 5 local iterations for the μ -step, and 2 global iterations. Thus, *a total of 21 iterations and 26 iterations are used to obtain emission intensity (i.e., $\mathbf{x}^2$) and attenuation density (i.e., $\boldsymbol{\mu}^2$), respectively.*

The ML method is initialized using $(\mathbf{x}^0)_j = \sum_{i=1}^I \frac{y_i}{I\hat{\alpha}_i}$ and $(\boldsymbol{\mu}^0)_j = 0.0214$, except that $e^{-(\mathbf{L}\boldsymbol{\mu}^0)_i}$ is replaced with $\alpha_i^0 = \frac{r_i}{b_i}(\frac{r_k}{r_r})$. As state in Section 3.3.1 and Section 3.3.2, $(\mathbf{x}^k)_j^0 = (\mathbf{x}^{k-1})_j$ and $(\boldsymbol{\mu}^k)_j^0 = (\boldsymbol{\mu}^{k-1})_j$.

5.1.2 EMLL Algorithm with Corrected Data

For the EMLL algorithm with corrected data, the iterative equation is given below:

$$x_j^{k+1} = x_j^k \sum_{i=1}^I \frac{\hat{y}_i P_{ij}}{(\mathbf{P}\mathbf{x}^k)_i}, \quad (5.1)$$

where $\hat{y} = \frac{y_i}{\hat{\alpha}_i}$. It is initialized as follows: $x_j^0 = \frac{\sum_{i=1}^I \hat{y}_i}{I}$ for all j . *We run 20 iterations of the EMLL algorithm with corrected data.*

5.1.3 LS Reprojection Method

To initialize the iteration in eq. (4.1), we use a uniform initial estimate: $\bar{\mu}_j^0 = 0.0214$ for all j . We run 20 iterations to get the LS estimate of $\boldsymbol{\mu}$, $\bar{\boldsymbol{\mu}}$. Then, we run 20 iterations of the algorithm shown in eq. (4.4). Thus, *the LS reprojection method requires 40 iterations to get an emission image.*

The total emission count, typical transmission scan count, and short transmission scan count are 1.5 million, 0.5 million and 0.125 million, respectively. The blank scan, duration, the typical transmission scan duration, and the short transmission scan duration are 60 minutes, 20 minutes, and 5 minutes, respectively. We simulate the ML method, LS reprojection method, and the EMMML algorithm with corrected data using typical transmission scan data with and without smoothing and the short transmission scan data with and without smoothing. In the next section, we show the results using non-smoothed typical transmission scan data.

5.1.4 Non-smoothed Typical Transmission Scan Data

We present the results using a non-smoothed typical transmission scan data in this section. The emission image of the cardiac emission phantom using the ML method after the 1st global iteration, 2nd global iteration, and 3rd global iteration are shown in Fig. 5.1 (b), Fig. 5.1 (c), and Fig. 5.1 (d), respectively. It can be seen that the emission images improve with increasing iteration. However, after 3 global iterations, the emission images become noisy and less accurate, which indicates that a stopping rule needs to be found. This problem is a common one for statistically based algorithms.

The reconstructions of the cardiac attenuation phantom using the ML method after the 1st global iteration, 2nd global iteration, and 3rd global iteration are shown in Fig. 5.2 (b), Fig. 5.2 (c), and Fig. 5.2 (d), respectively. In the attenuation images, the lungs are not visible, and only the contour and the spine can be seen. Also, there are artifacts outside the ROI.

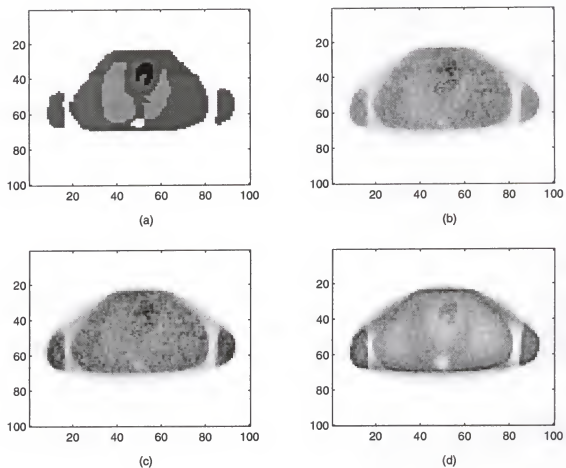


Figure 5.1. Reconstruction of cardiac emission phantom using non-smoothed typical transmission scan data (a) phantom (b) 1st global iteration (c) 2nd global iteration (d) 3rd global iteration

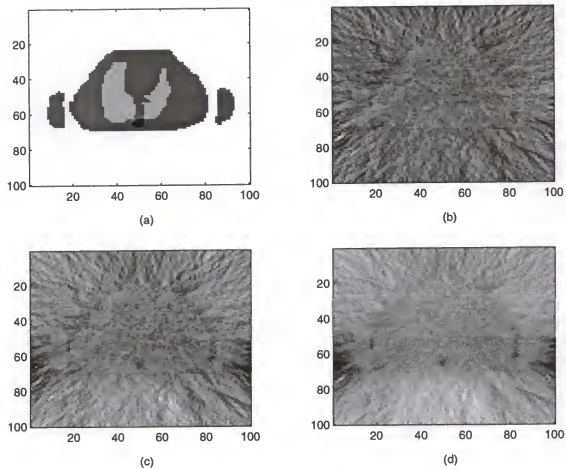


Figure 5.2. Reconstruction of cardiac attenuation phantom using non-smoothed typical transmission scan data (a) attenuation phantom (b) 1st global iteration (c) 2nd global iteration (d) 3rd global iteration

For the cardiac emission phantom, the results of the EMMML algorithm with corrected data, the LS reprojection method, and the ML method are shown in Fig. 5.3 (a), Fig. 5.3 (b), Fig. 5.3 (c), and Fig. 5.3(d), respectively. From this figure, it can be seen that the ML method yields an image with better contrast and resolution than the EMMML algorithm with corrected data and the LS reprojection method (note the lungs and the heart at the top center of the cardiac phantom). It also can be seen that the EMMML algorithm with corrected data does not successfully resolve either the lungs or the heart. In the emission image of the LS reprojection method, the spine can be seen clearly. However, the LS reprojection method also provides incorrect information as seen by the fact that the lungs have a higher activity concentration than the soft tissues around them (see the phantom in Fig. 5.3 (a)).

In Fig. 5.4, we show the line plots of the 50th row of the emission images in Fig. 5.3 . We observe that both the LS reprojection method and the EMMML algorithm with corrected data are more biased than the ML method (note the plot between 52 and 62, which is inside the right lung area). From this line plot, we find that the ML method not only produces emission images with better contrast but also gives a more accurate estimate of the emission intensity than other methods.

The EMMML algorithm with corrected data does not reconstruct attenuation images, so we only show the attenuation images of the ML method and the LS reprojection method in Fig. 5.5 (b) and Fig. 5.5 (c), respectively. The ideal attenuation phantom is shown in Fig. 5.5 (a). We can see that the attenuation density reconstruction of the ML method in Fig. 5.5 (b) has a lot of artifacts and

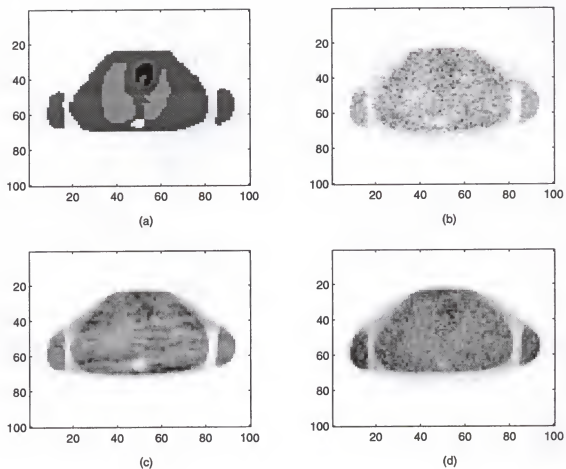


Figure 5.3. Reconstruction of cardiac emission phantom using non-smoothed typical transmission scan data (a) emission phantom (b) EMML algorithm with corrected data (c) LS reprojection method (d) ML method

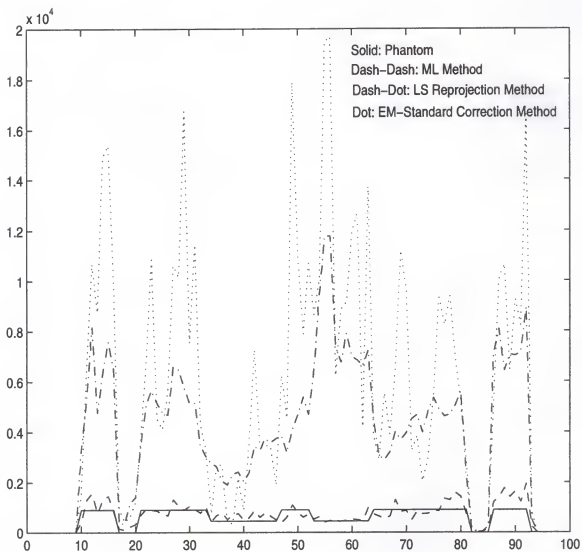


Figure 5.4. Line plot of the 50th row of the reconstruction of cardiac emission phantom using non-smoothed typical transmission scan data

does not resolve the lungs, spine, and soft tissue. The LS reprojection method resolves lungs and soft tissues but also has artifacts.

We also show the emission images of the ML method initialized with a LS estimate of the attenuation density. Since the μ -step is supposed to determine a better estimate of μ , we want to check if a better initial μ will correct the artifact problem of the attenuation images and provide better emission images for the ML method. In Fig. 5.6 (b), we can observe that spine is clearer, but the lung area is incorrect. However, the attenuation image in Fig. 5.6 (d) is better than Fig. 5.5 (b) (resolve lungs, soft tissue but no spine).

The results of the EMMML algorithm with corrected data, the LS reprojection method and the ML method using the chest phantom are shown in Fig. 5.7 (b), 5.7 (c), and 5.7 (d), respectively. From this figure, we can observe that the ML method and the LS reprojection method produce comparable emission images. Both images have better contrast and resolution than the EMMML algorithm with corrected data. Note, the emission image produced by the EM algorithm with corrected data is very noisy.

We present the attenuation images of the ML method and the LS reprojection method for the chest phantom in Fig. 5.8 (b) and Fig. 5.8 (c), respectively. The ideal attenuation phantom is shown in Fig. 5.8 (a). For the chest phantom, the ML method provides better contrast and more details (big and small spots in the center) than the LS reprojection method. The LS reprojection method fails to resolve any information.

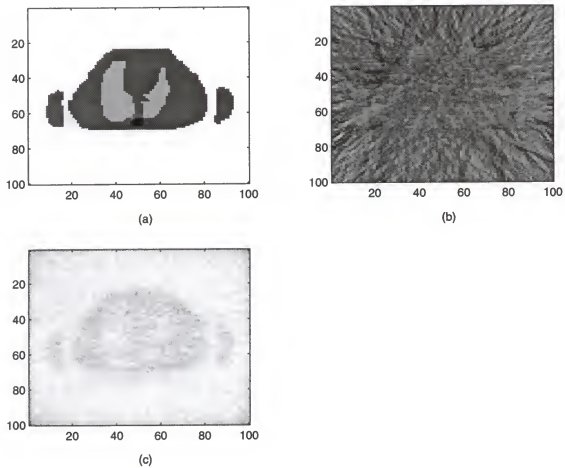


Figure 5.5. Reconstruction of cardiac attenuation phantom using non-smoothed typical transmission scan data (a) attenuation phantom (b) ML method (c) LS reprojection method

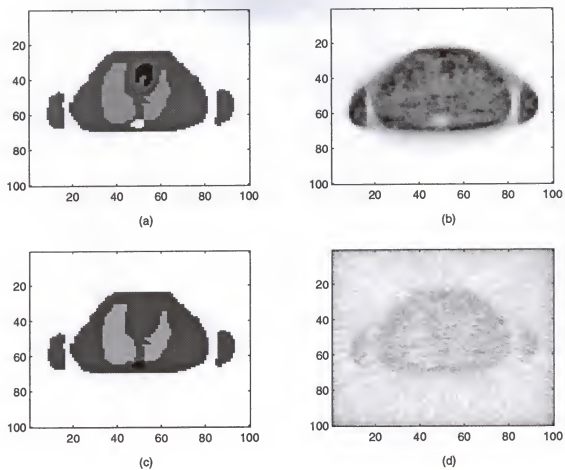


Figure 5.6. ML method (a) emission phantom (b) emission image (c) attenuation phantom (d) attenuation image

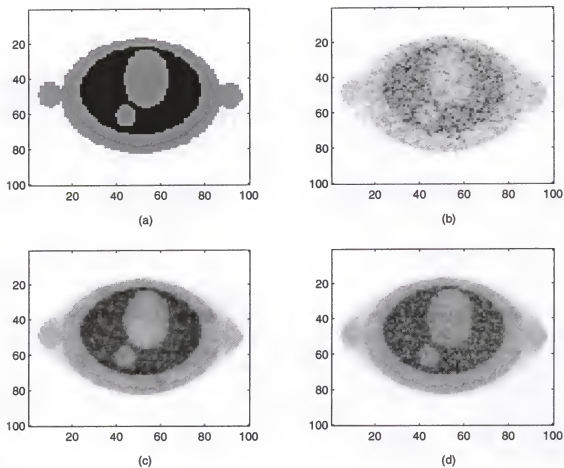


Figure 5.7. Reconstruction of chest emission phantom using non-smoothed typical transmission scan data (a) emission phantom (b) EMML algorithm with corrected data (c) LS reprojection method (d) ML method

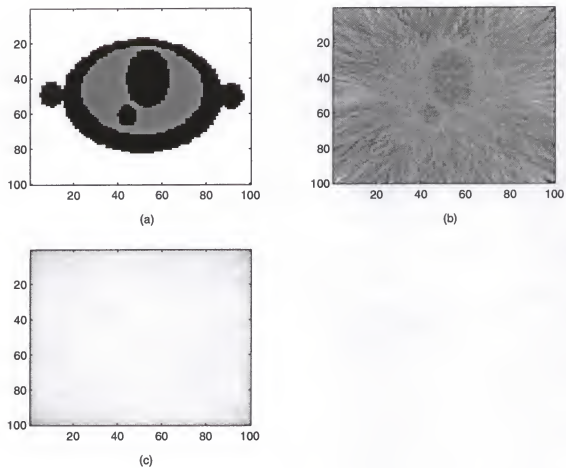


Figure 5.8. Reconstruction of chest attenuation phantom using non-smoothed typical transmission scan data (a) attenuation phantom (b) ML method (c) LS reprojection method

In practice, the transmission scan data is smoothed even though it is ad hoc to do so [34]. In next section, we show the results of the simulations using smoothed transmission scan data.

5.1.5 Smoothed Typical Transmission Scan Data

Since the survival probability estimated by the ratio of transmission scan data and blank scan data is usually noisy and biased, a popular way to address this problem is to smooth the transmission scan data [13, 34, 41]. We use a 1×3 box car filter, $[\frac{1}{3} \ \frac{1}{3} \ \frac{1}{3}]$ to smooth the transmission scan data.

We show the emission images of the EMMML algorithm with corrected data, the LS reprojection method and the ML method for the cardiac phantom using smoothed typical transmission scan data in Fig. 5.9 (b), 5.9 (c), and Fig. 5.9 (d), respectively. Note that the LS reprojection method resolves more details of the lungs, heart and the spine than the ML method. Both methods produce images much better than the EMMML algorithm with corrected data.

This study demonstrates that smoothing the transmission scan data improves the quality of the emission images. In order to compare the accuracy of the emission image, in Fig. 5.10, we show the line plots of the 50th row of the images in Fig. 5.9. We can see that the line plot of the LS reprojection method and the EMMML algorithm with corrected data both provide worse estimates of the emission intensity than the ML method.

We also compare the attenuation images. We show the result of the ML method and the LS reprojection method in Fig. 5.11 (b) and Fig. 5.11 (c), respectively.

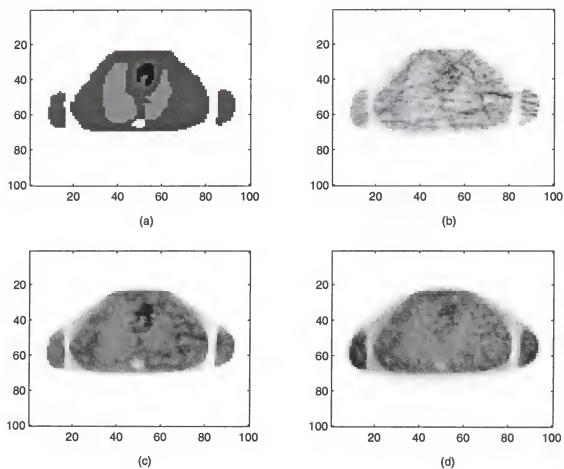


Figure 5.9. Reconstruction of cardiac emission phantom using smoothed typical transmission scan data (a) emission phantom (b) EMLL algorithm with corrected data (c) LS reprojection method (d) ML method

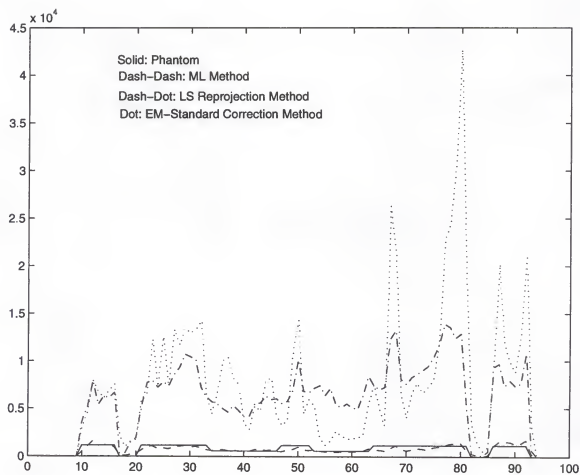


Figure 5.10. Line plot of the 50th row of reconstruction of cardiac emission phantom using the smoothed transmission scan data

The ML method still produces an attenuation image with heavy artifacts while the LS method provides an image with better contrast and quality. Compared to the attenuation images using non-smoothed transmission scan data in Fig. 5.5, both attenuation images show more features.

The emission and attenuation image of the ML method using an initial estimate for μ was obtained from the LS reprojection method are shown in Fig. 5.12 (b), Fig. 5.12 (d), respectively. The ML method produces emission image with better contrast in the heart area in than Fig. 5.9 (b). The attenuation image provides more information than both attenuation images in Fig. 5.11 (note the black spine at the center below).

The emission images of the EMM algorithm with corrected data, the LS reprojection method and the ML method of the chest phantom using smoothed typical transmission scan data are shown in Fig. 5.13 (b), 5.13 (c), and 5.13 (d), respectively. We can see that the LS reprojection method and the ML method produce comparable images. Both methods provide better contrast and the image quality than the EMM algorithm with corrected data.

The attenuation images of the ML method and the LS reprojection method using the typical smoothed transmission data for chest attenuation phantom are shown in Fig. 5.14 (b) and Fig. 5.14 (c), respectively. The ML method resolves lungs, a heart and soft tissue while the LS method fails to provide any information. The attenuation image of the ML method is smoother than Fig. 5.8 (b) but the contrast and quality do not improve.

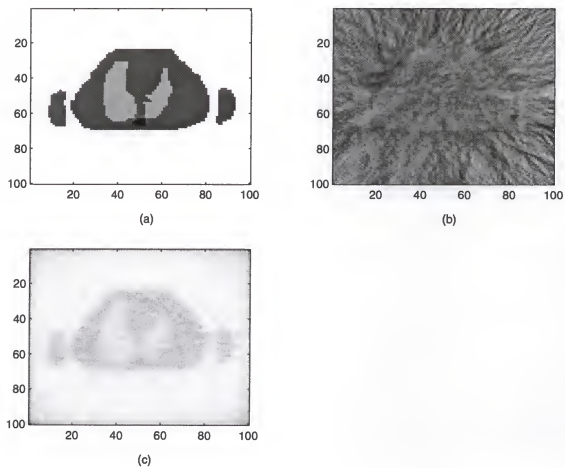


Figure 5.11. Reconstruction of cardiac attenuation phantom using the smoothed typical transmission scan data (a) attenuation phantom (b) ML method (c) LS reprojection method

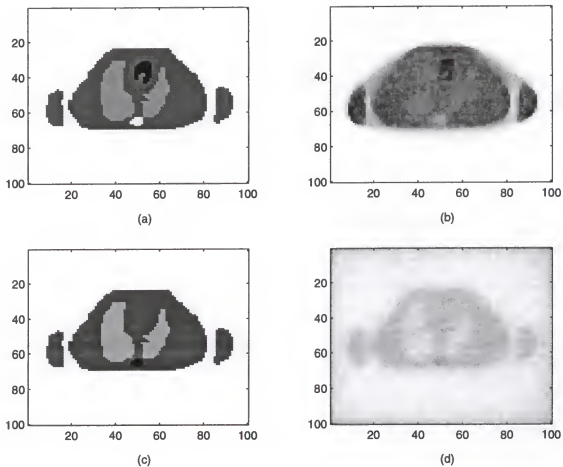


Figure 5.12. ML method (a) emission phantom (b) emission image (c) attenuation phantom (d) attenuation image

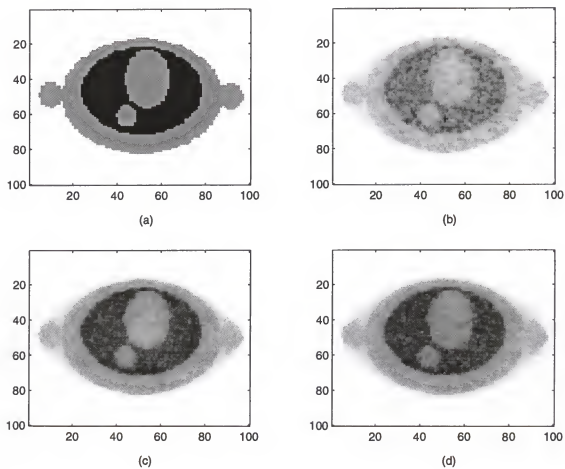


Figure 5.13. Emission image of the chest phantom using smoothed typical transmission scan data (a) emission phantom (b) EMML algorithm with corrected data (c) LS reprojection method (d) ML method

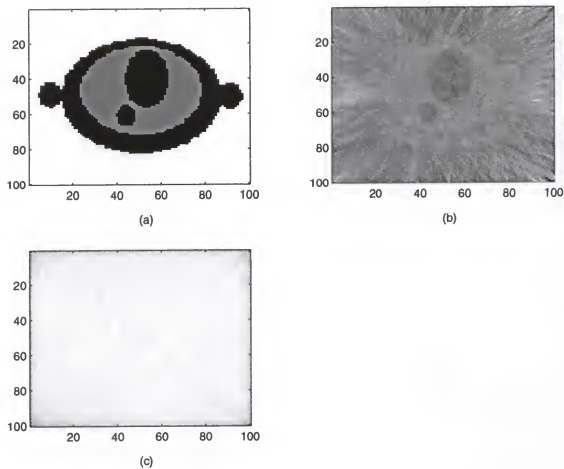


Figure 5.14. Reconstruction of chest attenuation phantom using smoothed typical transmission scan data (a) attenuation phantom (b) ML method (c) LS reprojection method

In order to compare the methods numerically, we compute their peak-signal-to-noise-ratio (PSNR) [43] for the different images. PSNR is defined by

$$\text{PSNR(dB)} = 10 \log_{10} \frac{x_{\text{peak}}^2}{mse}, \quad (5.2)$$

where x_{peak} is the peak value of the phantom, $mse = \frac{1}{J} \sum_{j=1}^J (x_j - \hat{x}_j)^2$, x_j is the j^{th} voxel in phantom, and $\hat{x}_j$ is an estimate of x_j . We compare the PSNR of the methods using the typical transmission scan data in Table 5.1. We can

dB	cardiac phantom			chest phantom		
Algorithm	Standard	ML	LS-Rep.	Standard	ML	LS-Rep.
Non-smooth	-7.5	12.51	-5.92	-6.3	12.73	-4.8
Smooth	-15.5	8.62	-5.62	-6.7	12.78	-4.56

Table 5.1. PSNR (dB) of emission images using typical transmission scan data

observe that the emission images of the ML method have the highest PSNR and the EMLL algorithm with corrected data has the lowest PSNR.

Another application of the proposed methods is the case of short duration transmission scan data. In the next two sections, we show the results using a 5 minutes short transmission scan data with and without smoothing.

5.1.6 Non-smoothed Short Transmission Scan Data

In this section, we show the results using a 5 minutes transmission scan. The emission images of the EMLL algorithm with corrected data, the LS reprojection method and the ML method of cardiac emission phantom using non-smoothed typical transmission scan data are shown in Fig. 5.15 (b), 5.15 (c), and 5.15 (d),

respectively. From this figure, we know that the ML method resolves the heart and lungs better than the the EMM algorithm with corrected data and the LS reprojection method. The emission image of the LS reprojection method produces incorrect information in the lungs region.

We also compare the attenuation images. We show the result of the ML method and the LS reprojection method in Fig. 5.16 (b) and Fig. 5.16 (c), respectively. We can see that the attenuation image of ML method in Fig. 5.16 (b) has a lot of artifacts and only resolves spine (black spot at the center below). The attenuation image of the LS reprojection method in Fig. 5.16 (c) shows the basic contours better than the ML method but also suffers from the artifacts. Both methods provide worse attenuation images when using short transmission scan data.

The emission and attenuation image of the ML method initialized using the LS estimate of μ are shown in Fig. 5.17 (b), Fig. 5.17 (d), respectively. The ML method resolves the heart area better than Fig. 5.15 (d) but produces the wrong information of the lungs. The attenuation image provides more information and less artifacts than Fig. 5.16 (c).

The results of the EMM algorithm with corrected data, the LS reprojection method and the ML method of chest emission phantom using non-smoothed short transmission scan data are shown in Fig. 5.18 (b), 5.18 (c), and 5.18 (d), respectively. From this figure, we can observe that the ML method that produces image with better contrast, resolution than the EMM algorithm with corrected data and the LS reprojection method. The EMM algorithm with corrected data and LS reprojection method both produce image with wrong information. The

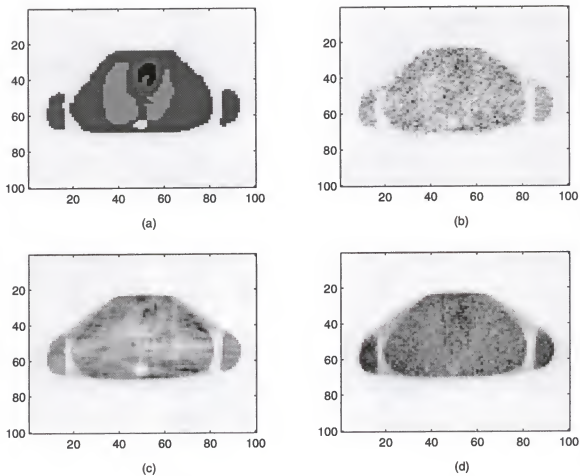


Figure 5.15. Reconstruction of cardiac emission phantom using the non-smoothed short transmission scan data (a) emission phantom (b) EMML algorithm with corrected data (c) LS reprojection method (d) ML method

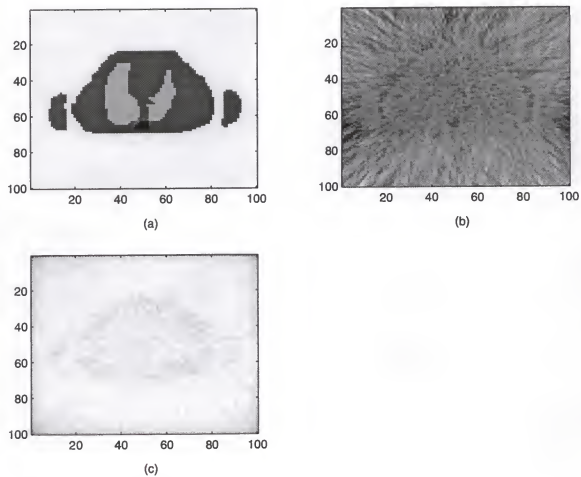


Figure 5.16. Reconstruction of cardiac attenuation phantom using non-smoothed short transmission scan data (a) attenuation phantom (b) ML method (c) LS reprojection method

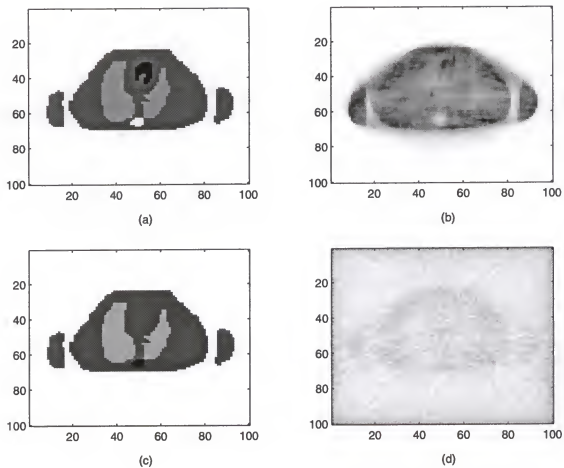


Figure 5.17. ML method (a) emission phantom (b) emission image (c) attenuation phantom (d) attenuation image

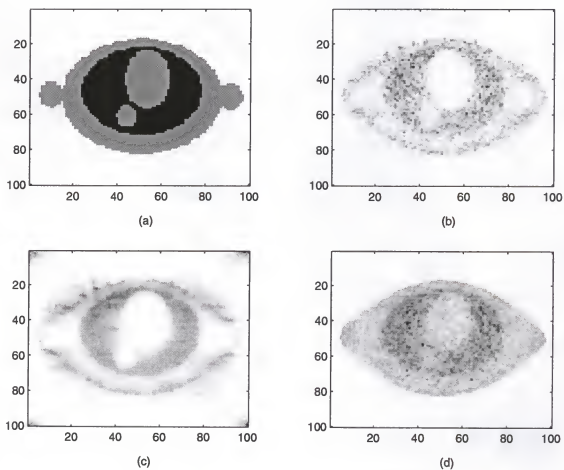


Figure 5.18. Reconstruction of chest emission phantom using non-smoothed short transmission scan data (a) emission phantom (b) EMMML algorithm with corrected data (c) LS reprojection method (d) ML method

emission image of the LS reprojection method is smoother than the one of the EMML algorithm with corrected data.

We present the attenuation images of the ML method and the LS reprojection method in Fig. 5.19 (b) and Fig. 5.19 (c), respectively. The LS method does not provide too much information while the ML method provides a noisy attenuation image. However, the ML method resolves the high density region at the center.

In the next section, we show the results of the simulations using smoothed short transmission scan data.

5.1.7. Smoothed Short Transmission Scan Data

In this section, we show the results with short transmission scan smoothed by the same 1×3 box car filter, $[\frac{1}{3} \ \frac{1}{3} \ \frac{1}{3}]$. The emission images of the EMML algorithm with corrected data, the LS reprojection method and the ML method of cardiac phantom using smoothed short transmission scan data are shown in Fig. 5.20 (b), 5.20 (c), and 5.20 (d), respectively. Again, we observe that We can see that the LS reprojection method provides the comparable emission image with the ML method in the sense of the contrast and image quality. Note that the LS reprojection method resolves more details of the lungs, heart and spine but also suffers from quantitative inaccuracy. Especially, the LS reprojection method provides clearer heart area than other methods. The ML method and the LS reprojection method both methods produce images much better than the EMML algorithm with corrected data.

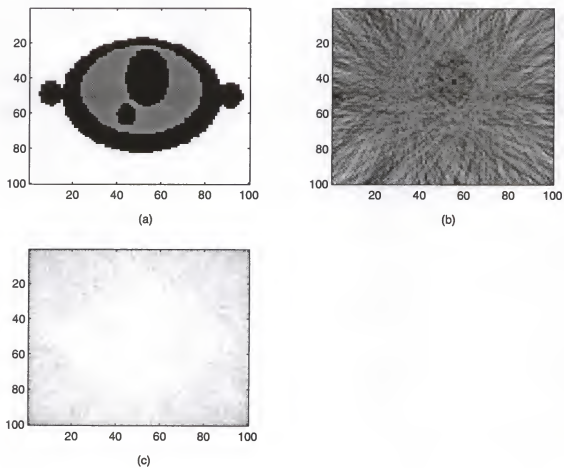


Figure 5.19. Reconstruction of chest phantom using non-smoothed short transmission scan data (a) attenuation phantom (b) ML method (c) LS reprojection method

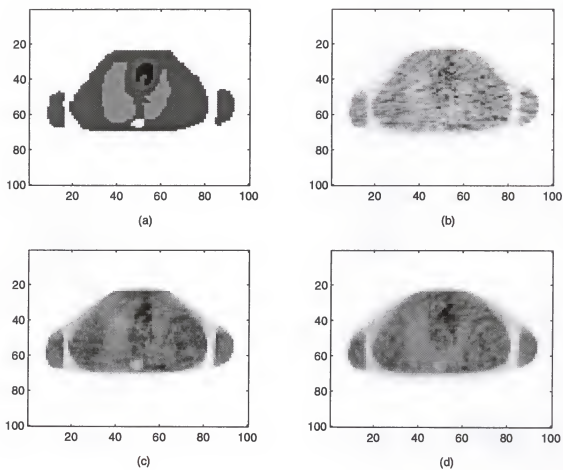


Figure 5.20. Reconstruction of cardiac emission phantom using smoothed short transmission scan data (a) emission phantom (b) EMLL algorithm with corrected data (c) LS reprojection method (d) ML method

We show the attenuation images of the ML method and the LS reprojection method in Fig. 5.21 (b) and Fig. 5.21 (c), respectively. The attenuation image of the LS method provides the shape of the attenuation map while the image of the ML method suffers from heavy artifacts.

The emission and attenuation image of the ML method initialized with $\bar{\mu}$ are shown in Fig. 5.22 (b), Fig. 5.22 (d), respectively. The ML method almost produces the best emission images for the all short transmission scan experiments. In particular, it provides a very clear reconstruction of the heart area (see Fig. 5.9 (b)).

The emission images of the EMMML algorithm with corrected data, the LS reprojection method and the ML method of the chest emission phantom using smoothed short transmission scan data are shown in Fig. 5.23 (b), 5.23 (c), and 5.23 (d), respectively. From this figure, we can observe that the ML method produces an image with more details than the other images (Note, the small high density spot area at the left below).

We present the attenuation images of the ML method and the LS reprojection method in Fig. 5.24 (b) and Fig. 5.24 (c), respectively. We can see that the ML method produces a more accurate attenuation image than the LS reprojection method fails to resolve anything (note the two spots at the center). Compared to the attenuation images using non-smoothed transmission scan data, attenuation images here have more details and features.

The comparisons of the PSNR for the emission images using the short transmission scan data are shown in Table 5.2. Again, the ML method has the largest PSNR. In the next section, we show the results using the real data.

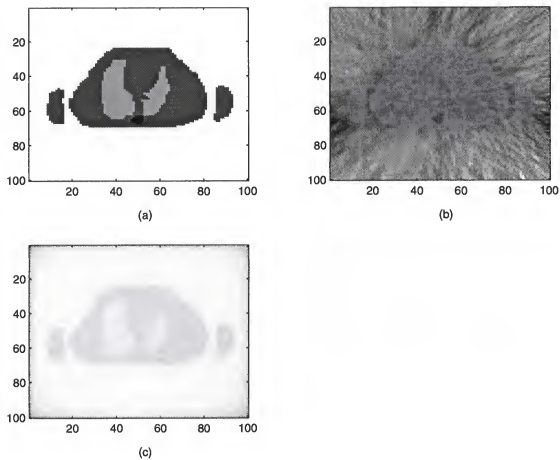


Figure 5.21. Reconstruction of cardiac attenuation phantom using smoothed short transmission scan data (a) attenuation phantom (b) ML method (c) LS reprojection method

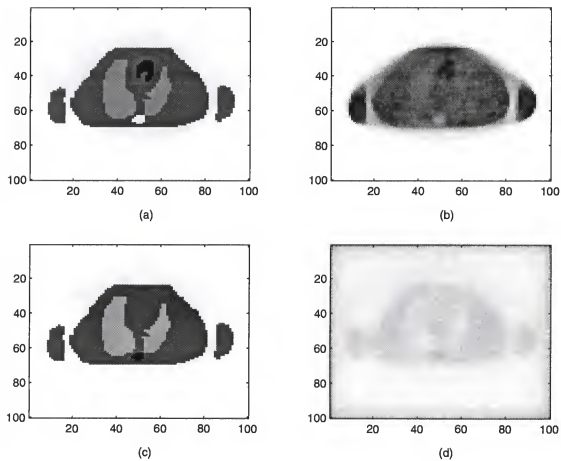


Figure 5.22. ML method (a) emission phantom (b) emission image (c) attenuation phantom (d) attenuation image

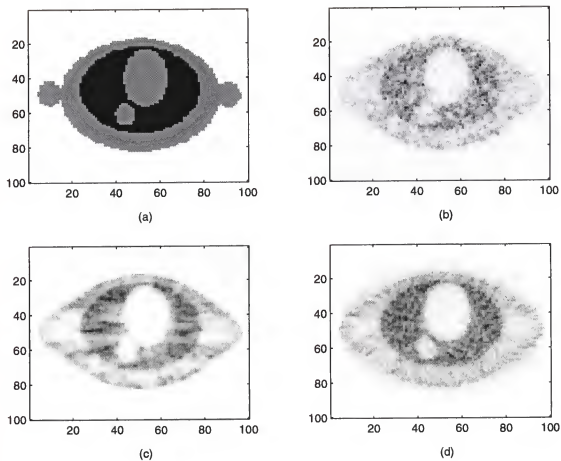
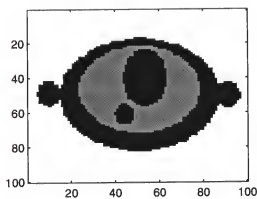
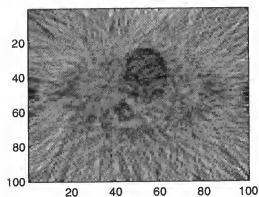


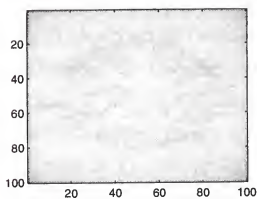
Figure 5.23. Reconstruction of chest emission phantom using smoothed short transmission scan data (a) emission phantom (b) EMML algorithm with corrected data (c) LS reprojection method (d) ML method



(a)



(b)



(c)

Figure 5.24. Reconstruction of chest attenuation phantom using smoothed short transmission scan data (a) attenuation phantom (b) ML method (c) LS reprojection method

dB	cardiac phantom			chest phantom		
Algorithm	Standard	ML	LS-Rep.	Standard	ML	LS-Rep.
Non-smooth	-13.9	22.13	-9	-5.8	10.33	9.28
Smooth	-13.62	19.85	-11	-15.2	9.02	-8.22

Table 5.2. PSNR (dB) of reconstruction of cardiac emission phantom using short transmission scan data

5.2 Real Data

We obtained real data from Dr. John Votaw, Associate Professor of Radiology at the Emory University Hospital. To create the data, a thorax phantom with a *hot* heart, two lungs, a spine, and soft tissue was scanned using the Siemens-CTI ECAT EXACT 921 PET scanner. This scanner is comprised of 24 rings of diameter 82.5 cm, where each ring contains 384 detectors of size 6.35×6.35 mm². In addition, the diameter of the scanner's patient port is 56.2 cm and its axial field of view is 16.2 cm. The field of view is a square where each side equals to 45 cm. There are $J = 128 \times 128$ voxels in the field of view. In two-dimensional mode, *virtual rings* are created by the cross-ring tubes. Since the ECAT EXACT scanner consists of 24 rings and 23 virtual rings, it provides 47 planes of data. Additional details on the scanner can be found in the paper of Wienhard et. al [53].

The duration of the emission scan, transmission scan, and blank scan are 25 minutes, 25 minutes, and 60 minutes, respectively. Associated with each plane are the sinograms for the emission data, transmission data, and the accidental coincidence data from the emission and transmission scan. The sinograms are of

size 160×192 corresponding to 192 angles with 160 bins per angle. The number of tube is $I = 73536$. In the next section, we discuss details of the implementation.

5.2.1 Overview of Implementation

All the images shown are for the 10th plane. This plane was chosen because it contains most of the major features of the thorax phantom. The 10th plane contains 0.288 million emission counts (i.e., $\sum_{i=1}^I y_i = 2.88 \times 10^5$) and 13.82 million blank scan counts. The number of counts for the low quality transmission scan is 0.615 million (i.e., $\sum_{i=1}^I r_i = 6.15 \times 10^5$), while the high quality transmission scan contains 3.67 million counts (i.e., $\sum_{i=1}^I r_i = 3.67 \times 10^6$). It should be noted that the transmission scans were automatically smoothed using the scanner's data processing algorithm. The emission and transmission data have been corrected for detector inefficiency and accidental coincidences using standard procedures, however, no scatter correction has been done.

For the ML method, we run 2 global iterations, 7 and 5 iterations for the x -step and μ -step, respectively. In other words, the ML method requires total 19 iterations and 24 iterations to get an emission image and an attenuation image, respectively. The initial estimate for x -step is $(x^0)_j = \sum_{i=1}^I \frac{y_i}{l\alpha_i}$ for all j , where $\hat{\alpha}_i = \frac{r_i}{b_i}(\frac{\tau_b}{\tau_r})$. The initial estimate for μ -step is $(\mu^0)_j = 0.07$ for all j . The initial estimate for the survival probability is $\alpha_i^0 = \frac{r_i \tau_b}{b_i \tau_r}$, where $\tau_b = 60$ minutes and $\tau_r = 25$ minutes.

Twenty iterations of the EMMML algorithm with corrected data method is initialized using $x_j^0 = \frac{\sum_{i=1}^I \hat{y}_i}{I}$ for all j , where $\hat{y}_i = \frac{y_i}{\alpha_i}$. For the LS reprojection method,

to initialize eq. (4.1), we use a uniform initial estimate: $\tilde{\mu}_j^0 = 0.07$ for all j . We run 20 iterations to get the LS estimate of μ , $\bar{\mu}$. Then, we run 20 iterations of the algorithm shown in eq. (4.4). Thus, *LS reprojection method requires total 40 iterations to get an emission image.*

The transmission scan is a high quality scan because it was performed long after the emission scan was done (no emission counts will be mis-registered as transmission counts).

5.2.2 Results

The emission images of the filtered back-projection method, the EMML algorithm with corrected data, the LS reprojection method, and the ML method are shown in Fig. 5.25 (a), Fig. 5.25 (b), Fig. 5.25 (c), and Fig. 5.25 (d), respectively. From this figure, we observe that the EMML algorithm with corrected data produces an image with clearer lungs boundaries of the other methods. Also, the ML method produces comparable but smoother image than the EMML algorithm with corrected data. The filtered back-projection method provides a noisy emission image with lots of artifacts everywhere.

Except the emission images of the filtered back-projection method, all emission images have a “ring” artifact outside the phantom (see Fig. 5.25 (c) and Fig. 5.25 (d)), which is not visible in the image using the EMML algorithm with corrected data because the limited gray level scales of the image (the heart area in Fig. 5.25 (b) has high intensity values compared to the background, so the “ring” artifacts on the background cannot be seen).

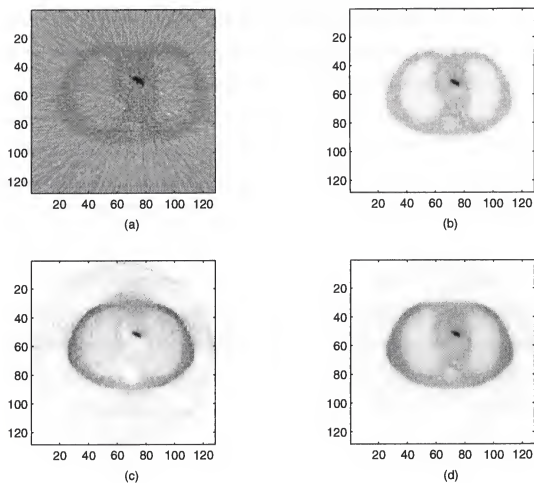


Figure 5.25. Emission images using high quality smoothed transmission scan data (a) Filtered back-projection method (b) EMLL algorithm with corrected data (c) LS reprojection method (d) ML method

The attenuation images of the ML method and the LS reprojection method are shown in Fig. 5.26 (a) and Fig. 5.26 (b), respectively. The attenuation image of the LS method in Fig. 5.26 (b) clearly delineates lungs, spine, and tissue regions, while the attenuation image of the ML method (see Fig. 5.26 (a)) still suffers from line artifacts. Additionally, the attenuation image of the ML method is influenced by the emission data (note the white spot at the center).

We also show the emission images of the EMMML algorithm with corrected data and the ML method using the non-smoothed transmission scan data in Fig. 5.27 (a) and Fig. 5.27 (b), respectively. The result of EMMML algorithm with corrected data becomes very noisy while the image of the ML method is still good.

To compare the computational complexity, we can observe that the ML method only takes 19 iterations to obtain its best image while the LS reprojection and the EMMML algorithm with corrected data requires 40 iterations and 20 iterations to obtain the best emission images, respectively. In other words, the ML method produces useful emission images and it has the less computational complexity than the EMMML algorithm with corrected data and the LS reprojection method.

In the next chapter, discuss our conclusion and possible research directions.

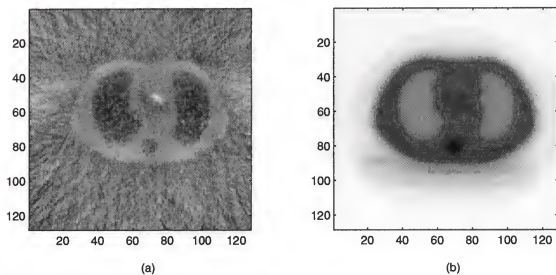


Figure 5.26. Attenuation images using high quality smoothed transmission scan data (a) ML method (b) LS reprojection method

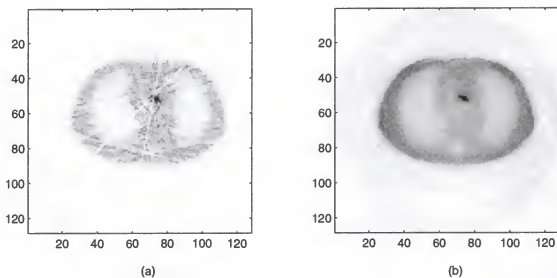


Figure 5.27. Emission image using high quality non-smoothed transmission scan data (a) EMML algorithm with corrected data (b) ML method

CHAPTER 6 CONCLUSIONS

In this dissertations, a ML method and a LS reprojection method were proposed for correcting attenuation in positron emission tomography. The ML method simultaneously estimates the emission intensity and the attenuation density. For the LS reprojection method, the attenuation density is first estimated using a least squares estimator. Then, this estimate is reprojected to estimate the survival probabilities, which are used to modify the probability matrix. Finally, the emission intensity is estimated using the EMML algorithm with the modified probability matrix.

In simulation studies, the proposed methods were compared to the EMML algorithm with corrected data using synthetic data and real data. Below, we sum up the advantages and disadvantages of the proposed methods:

- The ML method produces emission images with better contrast and more details with less computational complexity than the EMML algorithm with corrected data and the LS reprojection method when the short transmission scan data is used.
- The ML method provides more accurate emission images than the EMML algorithm with corrected data and the LS reprojection method

- The LS reprojection method produces comparable emission images but is less accurate than the ML method while the transmission scan data are smoothed.
- The LS reprojection method produces better attenuation images than the ML method for cardiac attenuation phantom.
- The ML method produces better attenuation images than the LS reprojection method for chest attenuation phantom.
- The EMMML algorithm with corrected data produces much better emission images when the transmission scan data is smoothed.

Given the performance of the proposed methods, it is felt that they will be most useful in short transmission scan protocols.

6.1 Future Work

The work in this thesis provides a new approach to correct the attenuation in PET. With the simulations using the real data obtained from the Emory University, the ML method steps in the real life application rather than the theoretical work. It provides an alternate tool for the medical society to use the research result in clinics. With more research done on searching different estimators and optimization algorithms such as the cyclic coordinate descent golden section method, the ML method can be expected to improve the emission images more. In addition, we may use the information from the histogram of the reconstruction of attenuation density to segment to the different mediums. Once we know where the different mediums distribute, we can assign the common attenuation density

values for air, water and bone. Then, we can use that information to get a better correction for attenuation.

The attenuation density reconstruction can be used to locate the different tissues such as bone, water and air within ROI by setting up the thresholds on the histogram of the attenuation density reconstruction images. Then, the known accurate attenuate density value can be assigned to the corresponding μ_j . And μ_j can be used to help improve the emission reconstruction.

For ML method, stopping rules for the x -step and the μ -step, the choice of the number of the global iteration to obtain the best emission images, the convergence of the algorithm, and the statistical analysis of the estimate are open issues. For LS reprojection method, a stopping rule, and the analysis of the algorithm also needs more investigation.

APPENDIX A

EMML Algorithm for PET

Shepp and Vardi used the EM algorithm [16] to obtain the ML estimate of the emission intensity for *error free data* [46]. In their formulation, the incomplete data is the observed data, $\mathbf{y}$, and the complete data is $\{N_{ij}\}$, where N_{ij} is the number of emissions in voxel j that are detected by tube i . Under the assumption that $\{N_{ij}\}$ are independent random variables and the assumptions in Section 2.2, the EM algorithm consists of the following steps. In the E-step, the expected value of the log likelihood function for the complete data given the incomplete data and the current estimate of the emission intensity is computed. Let L be the log likelihood of the complete data:

$$L(y_{11}, y_{12}, \dots, y_{1J}, \dots, y_{I1}, y_{I2}, \dots, y_{IJ}) \triangleq \log P(N_{11} = y_{11}, N_{12} = y_{12}, \quad (\text{A.1})$$

$$\dots, N_{1J} = y_{1J}, \dots, N_{I1} = y_{I1}, N_{I2} = y_{I2}, \dots, N_{IJ} = y_{IJ}) . \quad (\text{A.2})$$

$$U(\mathbf{x}, \mathbf{x}^k) \triangleq E[L(N_{11}, N_{12}, \dots, N_{1J}, \dots, N_{I1}, N_{I2}, \dots, N_{IJ}) | \mathbf{y}, \mathbf{x}^k, \mathbf{x}] \quad (\text{A.3})$$

$$= E\left[\sum_{i=1}^I \sum_{j=1}^J \{-P_{ij}x_j + N_{ij} \log(P_{ij}x_j)\} | \mathbf{y}, \mathbf{x}^k, \mathbf{x}\right] \quad (\text{A.4})$$

$$= \sum_{i=1}^I \sum_{j=1}^J \left\{-P_{ij}x_j + \frac{P_{ij}\hat{x}_j}{(\mathbf{P}\hat{\mathbf{x}})_i} y_i \log(P_{ij}x_j)\right\} . \quad (\text{A.5})$$

In the M-step, a new estimate for the emission intensity is obtained by maximizing $U(\mathbf{x}, \mathbf{x}^k)$ with respect to $\mathbf{x}$:

$$\mathbf{x}^{k+1} \triangleq \arg \max_{\mathbf{x} \geq 0} U(\mathbf{x}, \mathbf{x}^k) . \quad (\text{A.6})$$

Iterating back and forth between the E-step and M-step leads to the following iteration:

$$x_j^{k+1} = x_j^k \sum_{i=1}^I \frac{P_{ij} y_i}{(\mathbf{P} \mathbf{x}^k)_i}, \quad j = 1, 2, \dots, J, \quad (\text{A.7})$$

where x_j^k is the k^{th} estimate of x_j . This iteration is called the expectation maximization maximum likelihood (EMML) algorithm. Details on the EMML algorithm can be found in [46].

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John M.M. Anderson, Chairman
Associate Professor of Electrical and
Computer Engineering

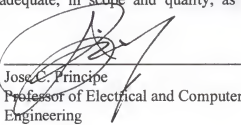
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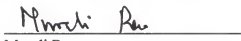
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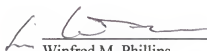

Jose C. Principe
Professor of Electrical and Computer
Engineering

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Murali Rao
Professor of Mathematics

This dissertation was submitted to the Graduate Faculty of the College of Engineering and to the Graduate School and was accepted as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

May 1998

A handwritten signature in dark ink, appearing to read 'W. M. Phillips', is written over a horizontal line.

Winfred M. Phillips
Dean, College of Engineering

Karen A. Holbrook
Dean, Graduate School

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